A.M.A. Archives of
OPHTHALMOLOGY

JANUARY 1956
VOLUME 55 NUMBER 1

The Changes in the Fundus of the Eye in Arterial Hypertension
Herman Elwyn

New Mercury Vacuum Pump and System of Slowly Applied Vacuum for Phakoerisis
Alfredo Villaseca

Epidermoid Carcinoma of the Lacrimal Sac
Robert J. Davis

Spear Cataract
Lt. Charles O. Parker Jr.

Diathermic Surgery for a Case of Angiomatosis Retinae
Bernard Kronenberg

The Spherophakia-Brachymorphia Syndrome
J. William Rosenthal and H. Warner Kloepfer

Ocular Manifestations of Systemic Cystinosis
David G. Cogan, Toichiro Kuwabara, Jin Kinoshita, David Sudarsky, and Henry Ring

Sarcoidosis of the Lacrimal Glands Associated with Sjögren's Syndrome
Capt. Ellis Gruber

Influence of Low-Voltage X-Radiation on Regression of Established Corneal Vessels
I. C. Michaelson and H. Schreiber

The Radioactive Phosphorus (P^{32}) Uptake Test in Ophthalmology
Irwin S. Terner, Irving H. Leopold, and Isadore J. Eisenberg

Further Studies of Effects of X-Radiation on Partially Shielded Lens of Rabbit
P. J. Leinfelder and E. F. Riley

Permanent Convergent Squint—Early Operation and Long-Term Follow-Up
W. Nordlöw

Mechanism of Serous Choroidal Detachment
Stanley A. Capper and Irving H. Leopold

Lids, Lacrimal Apparatus, and Conjunctiva
Alson E. Braley

COMPLETE CONTENTS ON FIRST PAGE

AMERICAN MEDICAL ASSOCIATION Publication

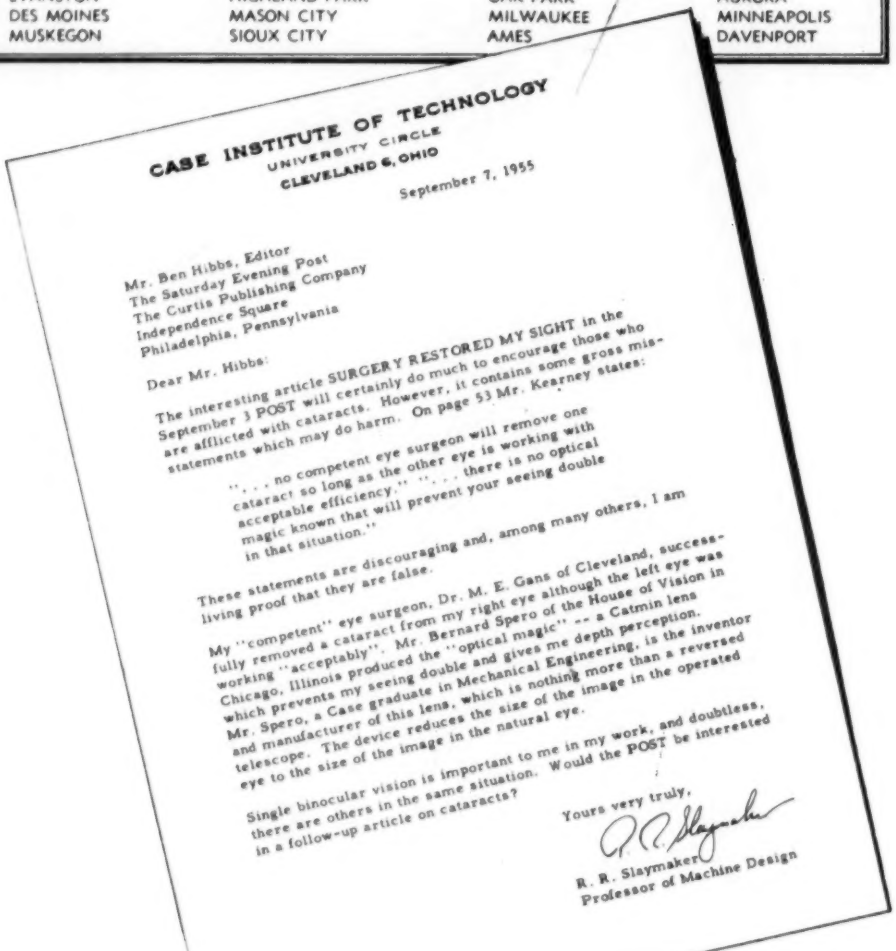
a scientific corner

FOR INFORMAL DISCUSSION OF YOUR OPTICAL PROBLEMS

The House of Vision Inc.

CHICAGO

EVANSTON	HIGHLAND PARK	OAK PARK	AURORA
DES MOINES	MASON CITY	MILWAUKEE	MINNEAPOLIS
MUSKEGON	SIOUX CITY	AMES	DAVENPORT



CASE INSTITUTE OF TECHNOLOGY
UNIVERSITY CIRCLE
CLEVELAND 6, OHIO

September 7, 1955

Mr. Ben Hibbs, Editor
The Saturday Evening Post
The Curtis Publishing Company
Independence Square
Philadelphia, Pennsylvania

Dear Mr. Hibbs:

The interesting article SURGERY RESTORED MY SIGHT in the September 3 POST will certainly do much to encourage those who are afflicted with cataracts. However, it contains some gross misstatements which may do harm. On page 53 Mr. Kearney states:

"... no competent eye surgeon will remove one cataract so long as the other eye is working with acceptable efficiency." "... there is no optical magic known that will prevent your seeing double in that situation."

These statements are discouraging and, among many others, I am living proof that they are false.

My "competent" eye surgeon, Dr. M. E. Gans of Cleveland, successfully removed a cataract from my right eye although the left eye was working "acceptably". Mr. Bernard Spero of the House of Vision in Chicago, Illinois produced the "optical magic" -- a Catmin lens which prevents my seeing double and gives me depth perception. Mr. Spero, a Case graduate in Mechanical Engineering, is the inventor and manufacturer of this lens, which is nothing more than a reversed telescope. The device reduces the size of the image in the operated eye to the size of the image in the natural eye.

Single binocular vision is important to me in my work, and doubtless, there are others in the same situation. Would the POST be interested in a follow-up article on cataracts?

Yours very truly,

R. R. Slaymaker
Professor of Machine Design

Doctor: Have you ever tried a Catmin lens for monocular aphakia?

TABLE OF CONTENTS

VOLUME 55 JANUARY 1956 NUMBER 1

EDITORIALS

Building Your Own Retirement Fund PAGE
Francis H. Adler, M.D., Philadelphia 1

ORIGINAL ARTICLES

The Changes in the Fundus of the Eye in Arterial Hypertension
Herman Elwyn, M.D., New York 3

New Mercury Vacuum Pump and System of Slowly Applied Vacuum for Phakoerisis
Alfredo Villaseca, M.D., Santiago, Chile 9

Epidermoid Carcinoma of the Lacrimal Sac
Robert J. Davis, M.D., Iowa City 21

Spear Cataract
Lt. Charles O. Parker Jr. (MC), U.S.N. 23

Diathermic Surgery for a Case of Angiomatosis Retinae
Bernard Kronenberg, M.D., New York 25

The Spherophakia-Brachymorphia Syndrome
J. William Rosenthal, M.D., and H. Warner Kloepfer, Ph.D., New Orleans 28

Ocular Manifestations of Systemic Cystinosis
David G. Cogan, M.D.; Toichiro Kuwabara, M.D.; Jin Kinoshita, Ph.D., David Sudarsky, M.D., and Henry Ring, M.D., Boston 36

Sarcoidosis of the Lacrimal Glands Associated with Sjögren's Syndrome
Capt. Ellis Gruber (MC), U.S.A.F. 42

Influence of Low-Voltage X-Radiation on Regression of Established Corneal Vessels
I. C. Michaelson, Jerusalem, and H. Schreiber, Haifa 48

The Radioactive Phosphorus (P^{32}) Uptake Test in Ophthalmology
Irwin S. Terner, M.D., M.Sc.; Irving H. Leopold, M.D., D.Sc., Philadelphia, and Isadore J. Eisenberg, M.D., Harrisburg, Pa. 52

Further Studies of Effects of X-Radiation on Partially Shielded Lens of Rabbit
P. J. Leinfelder, M.D., and E. F. Riley, Ph.D., Iowa City 84

Permanent Convergent Squint—Early Operation and Long-Term Follow-Up
W. Nordlöw, M.D., Vänersborg, Sweden 87

Mechanism of Serous Choroidal Detachment
Stanley A. Capper, M.D., M.Sc., and Irving H. Leopold, M.D., D.Sc., Philadelphia 101

CLINICAL NOTES, NEW INSTRUMENTS AND TECHNIQUES

Use of the Binocular Microscope in Eye Operations
Henri M. Dekking, M.D., Groningen, Netherlands 114

CASE REPORTS

Spontaneous Complete Absorption of a Cataractous Lens
Norman Corin, M.D., Jamaica, N. Y. 118

Visual Function Studies in a Case of Large Aberrant Vessels in the Macula
David Volk, M.D., Cleveland 119

ANNUAL REVIEWS

Lids, Lacrimal Apparatus, and Conjunctiva
Alson E. Braley, M.D., Iowa City 123

OBITUARIES

Jonas S. Friedenwald, M.D. 155

CORRESPONDENCE

Chorioretinitis Produced by Atomic Bomb Explosion
Jacques Landesberg, M.D., Brooklyn 158

REGULAR DEPARTMENTS

News and Comment 158

A. M. A.
ARCHIVES OF OPHTHALMOLOGY

VOLUME 55 JANUARY 1956 NUMBER 1

COPYRIGHT, 1956, BY THE AMERICAN MEDICAL ASSOCIATION

Continuing the Publication
FOUNDED BY HERMAN KNAPP, 1869

EDITORIAL BOARD

FRANCIS HEED ADLER, Chief Editor
313 South Seventeenth Street, Philadelphia 3

WILLIAM ZENTMAYER, Philadelphia
W. L. BENEDICT, Rochester, Minn.
KENNETH C. SWAN, Portland, Ore.
WILLIAM F. HUGHES Jr., Chicago
DAVID G. COGAN, Boston
JONAS S. FRIEDENWALD, Baltimore
JOHN H. DUNNINGTON, New York

ASSOCIATES:

Alson E. Braley
F. Phinizy Calhoun Jr.
A. Gerard DeVoe
Trygve Gundersen
Joseph S. Haas
John E. Harris
John M. McLean
Paul W. Miles
Frank Payne
Ludwig von Sallmann
Henry P. Wagener
Maynard C. Wheeler

AUSTIN SMITH, Editor, A. M. A. Scientific Publications
GILBERT S. COOPER, Managing Editor, Specialty Journals

Published Monthly by

AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

Entered as Second Class Matter Feb. 7, 1929, at the Postoffice at Chicago, Under the Act of March 3, 1879. Annual Subscription, $12.00

ALL PLASTIC

ARTIFICIAL EYES

Individually Created

DAVID A. GROSSBERG INC.
133 EAST 58th STREET NEW YORK 22, N. Y
WICKERSHAM MEDICAL BLDG.

HydroCortone®

(HYDROCORTISONE, MERCK)

"...effective in some cases in which cortisone was comparatively ineffective..."[1]

MAJOR ADVANTAGES: Greater anti-inflammatory action than cortisone; smaller doses produce equivalent therapeutic response.

In the treatment of ocular disease, HYDROCORTONE "has proved effective in some cases in which cortisone was comparatively ineffective."[1] "The ideal treatment schedule in any severe intraocular inflammation, especially of the posterior segment, consists of an initial course of systemic therapy."[1] When the condition improves, local therapy may be adequate for control.

"Approximately 60 mg. daily has proved to be a good maintenance dose in chronic cases. There has been a surprising freedom from side effects such as Cushing's syndrome."[1]

INDICATIONS: Anterior segment inflammatory eye diseases and posterior segment inflammatory eye diseases.

SUPPLIED: ORAL—HYDROCORTONE Tablets: 20 mg., bottles of 25, 100, and 500 tablets; 10 mg., bottles of 50, 100, and 500 tablets; 5 mg., bottles of 50 tablets. **OPHTHALMIC**—Sterile Suspension of HYDROCORTONE Acetate: 0.5% and 2.5%, 5-cc. vials. Ophthalmic Ointment of HYDROCORTONE Acetate: 1.5%, 3.5-Gm. tubes.

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF MERCK & CO., INC.

REFERENCE: 1. Gordon, D.M., *Am. J. Ophth.* **37**:533, April 1954.

Instructions to Contributors

Communications regarding editorial management, subscriptions, reprints, etc., should be addressed to Specialty Journals, American Medical Association, 535 North Dearborn Street, Chicago 10.

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor of the Specialty Journal concerned. Articles are accepted for publication on condition that they are contributed solely to that journal.

An original typescript of an article should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. A carbon copy should be retained by the author. An article in English by a foreign author should be accompanied by a draft in the author's mother tongue. Improvised abbreviations should be avoided.

The main title of an article may not contain more than seventy characters and spaces; a subtitle may be of any length. The subtitle should be sufficiently detached from the main title that a punctuation mark as strong as a colon can be used in the Table of Contents to separate it from the main title; it must not begin with "with."

The author's name should be accompanied by the highest academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

A Case Report must be preceded by an introductory paragraph containing at least thirty words before the details of the case are given. To avert the possibility of legal action, patients' initials and hospital case numbers should not be published.

Material quoted from another publication must be quoted exactly if the original is in English—spelling, capitalization, punctuation, etc., unchanged. Material taken largely from another publication must be credited to the original author, whether quoted exactly or merely abstracted.

Each article should be accompanied by a summary in the present tense, presenting the main points of the article, but in somewhat more generalized terms than in the article itself.

If it is necessary to publish a recognizable photograph of a person, the photograph must be accompanied by written permission of the subject himself if an adult, or of the parents or guardian if a child, to publish his photograph. An illustration which has been published in another publication must be accompanied by written permission from the author and the original publisher to reproduce it in an A. M. A. Specialty Journal.

The maximum illustration allowance is ten illustrations within a total of 100 sq. inches or $100, whichever is of greater advantage to the author. When no restrictions are placed by the author upon cropping, reducing, and grouping, the publisher is often able to use twenty or more illustrations in one article with the $100 allowance. See an issue of this journal for examples. Oversized originals should be photographed and a print submitted. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author.

Any cut-off marks should be made on the margins (or mountings) rather than on the illustration itself. Charts and drawings should be in black ink on hard, white paper. Lettering must be large enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, an abbreviated title of the article, and top plainly indicated. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be numbered in the order in which they are referred to in the text or listed in alphabetical order without numbers. A chronological arrangement, with all entries for a given year alphabetized according to the surname of the first author, may be used if preferred. References should be typed on a special page at end of manuscript. They should conform to the style of the Quarterly Cumulative Index Medicus, and must include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. Names of periodicals should be given in full or abbreviated exactly as in the Quarterly Cumulative Index Medicus. Reference to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication. Titles of foreign articles, if originally in a generally known Romance or Germanic tongue, must either all be in English translation or all be in the original language. Titles in other languages must be translated. The author must assume responsibility for the accuracy of foreign titles.

Matter appearing in the A. M. A. Specialty Journals is covered by copyright, but as a rule no objection will be made to its reproduction in a reputable medical journal if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the A. M. A. Specialty Journals, or in any other publications issued by the Association, will not be permitted.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**

Now you can do a visual field examination in 5 minutes!

(Developed by
David O. Harrington, M. D.
and Milton Flocks, M. D.)

The new Multiple Pattern Field Screener provides a simple, rapid screening test for visual field defects.

The Screener contains ten cards which test specific areas of the visual field during quarter-second black light flashes. Results are remarkably accurate.

Write for complete information at no obligation.

priced at only **$185**

Jenkel-Davidson
OPTICAL COMPANY

366 POST STREET • SAN FRANCISCO, CALIFORNIA

VOLUME FILES
for
A.M.A. SPECIALTY JOURNALS

$1.50 a pair
as illustrated here (not suitable for foreign mailing)

Archives of Dermatology
Archives of Neurology and Psychiatry
Archives of Internal Medicine
Archives of Pathology
Archives of Surgery
Archives of Ophthalmology
Archives of Otolaryngology
American Journal of Diseases of Children
Archives of Industrial Health

You keep your Specialty Journals, of course, but where? Are they filed chronologically, in a convenient place — readily accessible for reference? Are they preserved for succeeding years?

The volume file cases shown above are inexpensive and serviceable. More important to you—when used with the indexes published each year, they make the Specialty Journals a valuable part of your permanent reference library. The files are sold only in pairs, one for each six issues (one volume) of a Specialty Journal. The two cases, or one pair, hold the twelve copies for one year.

Made of heavy fiberboard, cloth-taped at corners for extra strength. Covered with fine-quality binders cloth. Open at back and labelled on front for ready reference. Labels are supplied free—volume and year to be filled in as desired. When ordering specify title of Specialty Journal wanted on label.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street Chicago 10, Illinois

Wide Application in Ophthalmology

Neo-Synephrine hydrochloride ophthalmic viscous solution 10%

spreads evenly
adherent
clear
stable

CONJUNCTIVITIS

1/8% solution.

For rapid relief of congestion, itching, smarting and lacrimation.

REFRACTION, OPHTHALMOSCOPY

2.5% solution.

For prompt and short acting mydriasis virtually free from cycloplegia.

UVEITIS, POSTERIOR SYNECHIAE

10% solution (plain or viscous) or 10% emulsion.

For freeing recently formed posterior synechiae as well as for prevention of synechiae formation in uveitis (with atropine).

GLAUCOMA (certain cases and tests)

10% solution (plain or viscous), 10% emulsion or 2.5% solution.

For temporary reduction of intra-ocular tension and for the provocative test for angle block.

SURGERY

2.5% solution or 10% solution (plain or viscous).

For short acting powerful mydriatic effect, applied 30 to 60 minutes preoperatively.

NEO-SYNEPHRINE®
HYDROCHLORIDE

Winthrop LABORATORIES
NEW YORK 18, N. Y. • WINDSOR, ONT.

Neo-Synephrine, trademark reg. U. S. Pat. Off.
brand of phenylephrine

LENSOMETER

for accuracy . . .

LENSOMETER gives the critical accuracy you need over the entire range of measurements.

for dependability . . .

LENSOMETER has the superior design, workmanship, and materials to stand up under long, hard usage that would often cause less accurate devices to become inoperative.

for convenience . . .

LENSOMETER is easy to read, simple to operate, requires no involved calculations.

for versatility . . .

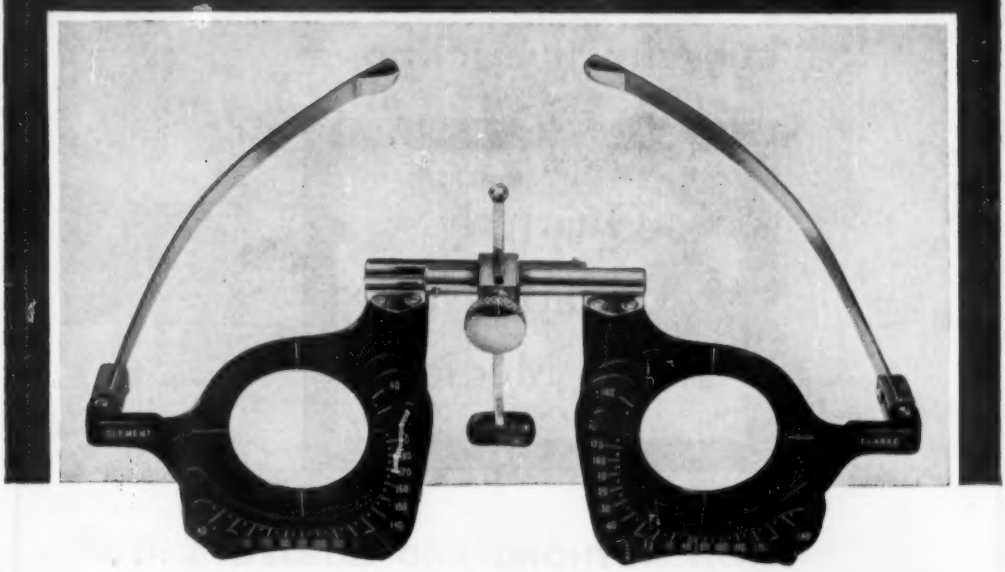
LENSOMETER accommodates high or low Rx in single vision, bifocal, trifocal or cataract lenses.

Only American Optical Company makes the LENSOMETER. For complete satisfaction now and in the years to come, accept no substitutes. A convincing demonstration of LENSOMETER superiority will gladly be arranged by any AO Office.

American Optical

INSTRUMENT DIVISION
BUFFALO 15, NEW YORK

Clement Clarke Present



THE SKEOCH TRIAL FRAME

This new trial frame has been designed to facilitate the ever-growing use of reduced aperture trial lenses, mounted in thin aluminium or plastic rims. The Skeoch has none of the drawbacks of many hitherto popular trial frames, and will prove to be of material assistance in refraction. It is simple, rigid, light in weight, and the comfort of the patients, including very young children, has not been overlooked. The features of the Skeoch trial frame are as follows :—

Lightness in weight (approximately 1½ ozs.). Apart from the sides, connecting bar and nosepiece, the frame is made of an aluminium alloy noted for strength and lightness. The sides are of hardened and tempered spring steel, the connecting bar is of nickel and the nosepiece is of plastic.

Shape and finish of nasal portions of cells, enabling frame to rest comfortably on patient's nose. For young children with very small interpupillary distances the frame will support itself on the sides of the nose without the aid of the bridge.

Contour of cells enabling lenses to be inserted and withdrawn with great ease, and cylinders to be rotated by a single thumb and finger movement.

Close spacing of cells, ensuring correct positioning of lenses and the absence of large gaps between them.

Extremely accurate engraving on the axis scales ensures correct positioning of cylinders. Crossline engraving facilitates the centration of frame in relation to pupils.

Angling sides of spring steel, to allow correct positioning of frame.

Two types available. 3 cell type for refractionists with a fully comprehensive trial case from which one lens only need be selected to correct the spherical error. 4 cell type recommended for those refractionists with a standard trial case from which 2 spheres are often required.

For illustrated leaflet on other Trial Frames please write to

CLEMENT CLARKE of England

INSTRUMENT DEPARTMENT: 63 WIGMORE STREET, LONDON, W.1.

YOUR GUIDE TO CURRENT PUBLICATIONS

Quarterly Cumulative Index Medicus

WITH AUTHORS AND SUBJECTS . . .

Divided into sections, one devoted to books and the other to periodical literature, the QUARTERLY CUMULATIVE INDEX MEDICUS contains a list of current publications alphabetized as to authors and subjects. The exact bibliographic reference is given under the author with titles in the original language, while titles under subjects are all in English. The index also includes a listing of journals, addresses and publishers.

The QUARTERLY CUMULATIVE INDEX MEDICUS appears twice a year; volumes are cloth bound and cover periodicals for six months as indicated on the publication. These two volumes will be a convenient and inclusive reference for current medical literature. Invaluable for practitioners, specialists, teachers, editors, writers, investigators, students and libraries.

SUBSCRIPTION PRICE $25.00 PER YEAR
CANADIAN AND FOREIGN $27.00 PER YEAR

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

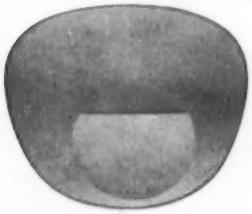
So near—but yet so far!

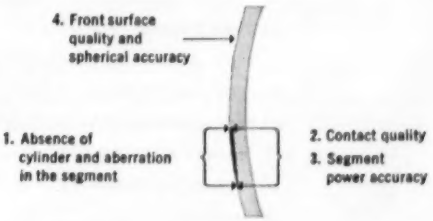
Father of a friend of ours used to tell about the man with the wonderful monkey. Truly an accomplished beast, he emulated human antics to perfection and enjoyed a successful stage career. Nightly, dressed in top hat and tails, the monkey would walk erect out to his waiting limousine and, door held open, would get down on *all fours* to climb into the car.

Many straight-top lenses have been "trained" to simulate Univis in appearance. But when it comes to the four inherent quality factors which are the sole responsibility of the manufacturer, these lenses often "get down on all fours".

We're proud of the care and skill with which Univis laboratories process prescriptions. We're proud, too, that more and more laboratories choose multifocals for the consistent quality of the four factors illustrated here. That's where Univis multifocals shine!

Corrected curves, of course; and thin segments, too!




4. Front surface quality and spherical accuracy
1. Absence of cylinder and aberration in the segment
2. Contact quality
3. Segment power accuracy

THE UNIVIS LENS COMPANY · DAYTON, OHIO

UNIVIS

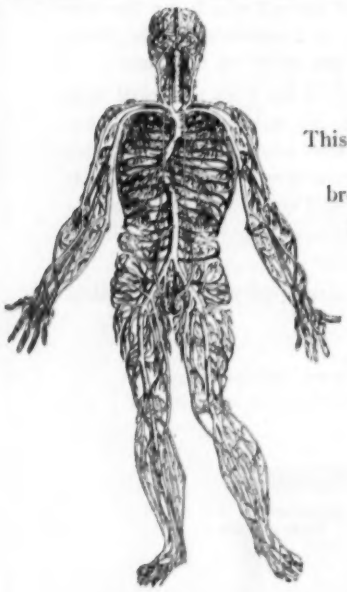
"LACRILENS"®

is a safe lens

The test of time proves that the "LACRILENS"® contact lens can be worn for long periods of time in aphakia and in all sports, including swimming. *Write For Brochure*

Obrig Laboratories Inc.
49 East 51st Street, New York 22, N. Y.

Manufacturers of all types of Contact Lenses
Branches in
PHILADELPHIA • MONTREAL • JOHANNESBURG



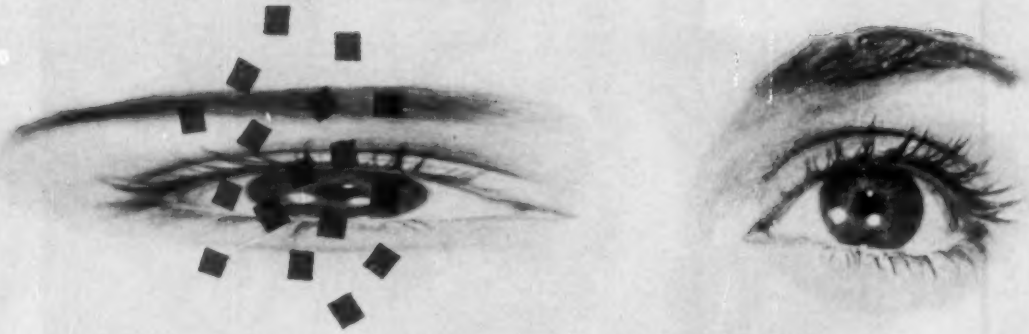
the human body

This series entitled "Wonder Stories of the Human Machine" will be helpful in answering some of the questions brought to you by patients. These pamphlets tell how the principal organ systems of the body work.

I **THE FRAMEWORK** (Bones)
II **THE RUNNING GEAR** (Muscles)
III **BREATHER PIPES AND THERMOSTATIC CONTROL** (Lungs and Skin)
IV **THE ENGINE** (Heart)
V **THE ELECTRIC SYSTEM** (Nerves)
VI **THE FUEL SYSTEM** (Digestion)
VII **THE EXHAUST** (Waste Removal)
VIII **SAFETY DEVICES** (The Sense Organs)
IX **THE BODY FINISH** (The Skin)
X **UPKEEP** (Healthy Living)

EACH 15 CENTS; SET OF TEN, $1.25
SEND YOUR REMITTANCE TO:

AMERICAN MEDICAL ASSOCIATION • 535 NORTH DEARBORN • CHICAGO 10



clearer prospect

Modern topical therapy brings a notably clearer prospect for rapid recovery from eye disturbances of infectious, inflammatory or allergic nature. Two leading broad-spectrum antibiotics (Tetracyn, Terramycin) and an outstanding anti-inflammatory hormone (Cortril) are potent and fast-acting, yet gentle to ocular tissues. They may be used singly or in combination.

TETRACYN® *(brand of tetracycline)* OPHTHALMIC OINTMENT (5 mg. tetracycline / Gm.) in ⅛ oz. tubes

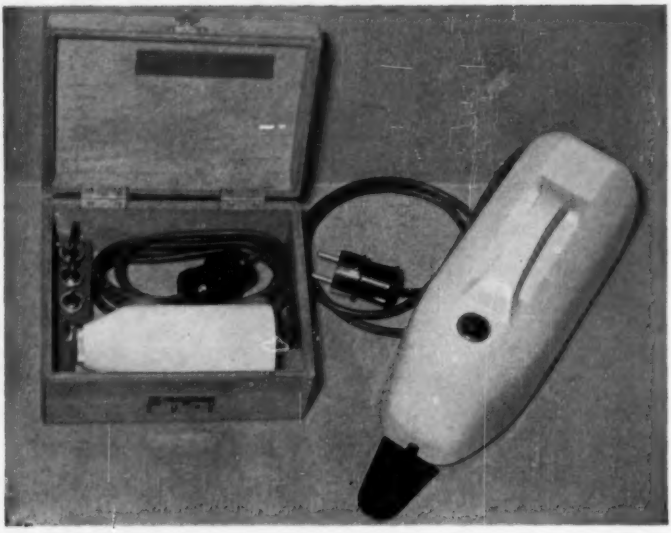
TERRAMYCIN® *(brand of oxytetracycline)* OPHTHALMIC OINTMENT WITH POLYMYXIN B SULFATE (5 mg. of oxytetracycline and 10,000 units of polymyxin B sulfate / Gm.) in ⅛ oz. tubes; OPHTHALMIC (FOR SOLUTION) 25 mg. oxytetracycline in 5 cc. dropper vials

CORTRIL® *(brand of hydrocortisone)* OPHTHALMIC OINTMENT (5 mg. hydrocortisone acetate / Gm.) in ⅛ oz. tubes and (25 mg. hydrocortisone acetate / Gm.) in ½ oz. tubes

Pfizer PFIZER LABORATORIES, *Division, Chas. Pfizer & Co., Inc.*, Brooklyn 6, N.Y.

storz
Surgical Instruments

NEW • LIGHT • POWERFUL



STORZ ATLAS **Hand Eye Magnet**

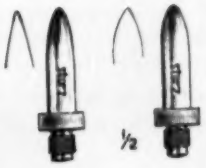
E-6650—Eye Magnet, Atlas: complete with four tips in wooden case and separate rectifier with footswitch. Small size for maneuverability and ease of handling. The magnet weighs 4.6 lbs. The rectifier with footswitch weighs 8.7 lbs. The type of tip selected is dependent on the position of the splinter. For strongest pulling power, the large cone tip is applied. More effective results are obtained by stepping on the footswitch repeatedly to get short interrupted pull rather than a long steady pull.

Power: The absolute pulling power at the flange is 12.5 kg. or 28 lb. The ball jump power is 38.5 mm. The handling is not interfered with by strong directional pulls.

Advantages... **Small size—Light weight—POWER! —**

Made for 110 volt, 60 cycle, alternating current. If other current or voltage is desired, please specify. Uses 150 watts. Developed and tested at the University Eye Clinic in Kiel.

Complete—$149.50



E-6654 Magnet Tip, Intra-ocular, BONACCOLTO: small. $3.75

E-6655 Magnet Tip, Intra-ocular, BONACCOLTO: large. $3.75

These tips not included with magnet. Please order separately.

Storz instruments are available from Storz salesmen only. We do not distribute under any other name or trademark.

Order directly from

Storz Instrument Company

4570 Audubon Ave. St. Louis 10, Mo.

MODERN D-25

More expensive...*and worth it!*

Threshold-Welded . . . Akro seg glass . . . thin, gray, non-reflecting angled segment top . . . corrected curves, of course . . .

by MODERN OPTICS *Incorporated*

SAN FRANCISCO HOUSTON CLEVELAND

TIME is your main problem in Routine Refractions...

CYCLOGYL®

HYDROCHLORIDE

(Brand of cyclopentolate hydrochloride)

saves time

FOR YOUR PATIENTS... FOR YOU...

ONLY THIRTY MINUTES' waiting time... and the patient is ready![1]

SAME DAY RECOVERY is obtained . . . Patients regain sufficient accommodation for reading within 4-12 hours, twice as fast with the use of a miotic preparation.[1]

USED ROUTINELY IN OFFICE AND HOSPITAL... Greater economy (fewer drops needed) and greater speed make CYCLOGYL a drug of choice for routine cycloplegia in both office and hospital practice. CYCLOGYL facilitates routine handling of even large groups of out-patients. "Apparently, it is relatively nonirritating and nonsensitizing during local application."[2] Patients can be assured that, except for the day of their examination, no time will be lost from work.[3]

DOSAGE: Cycloplegia — two drops of 0.5% or one drop 1.0%. In deeply pigmented eyes, two drops of 1.0% instilled 10 minutes apart. Mydriasis — see literature in package (literature on request).

SUPPLIED: Sterile ophthalmic solution in Gifford's Buffer (pH 6.0), with benzalkonium chloride as preservative agent. 0.5% Solution — 15 cc dropper bottles; 1.0% Solution — 15 cc and 2 cc dropper bottles.

1. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34 (July) 1955.
2. Council on Pharmacy and Chemistry, A.M.A.: New and Nonofficial Remedies, Philadelphia, J. B. Lippincott Company, 1955, p. 263.
3. Gettes, B. C.: A.M.A. Arch. Ophth. *51*:467 (April) 1954.
4. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. *38*:831 (Dec.) 1954 (a review of 8 studies covering 1035 patients).

SAMPLES ON REQUEST

Schieffelin & Co.

Pharmaceutical and Research Laboratories since 1794
28 Cooper Square, New York 3, N. Y.

Editorials

BUILDING YOUR OWN RETIREMENT FUND

An editorial in the April 24, 1954, issue of the *Saturday Evening Post* relates the story of a Philadelphia physician enjoying a large private practice who retired to accept a job in a government hospital, since he found he was unable to educate his children and at the same time save enough to provide for his eventual retirement under the existing tax laws for self-employed individuals. As an employee, he was eligible to participate in a pension plan which would provide him with a retirement income. The *Post* pointed out that a young doctor or lawyer, under our existing tax structure, was likely to find it impossible to put aside savings after taxes to provide for his old age. The professional man, like everyone whose income fluctuates widely over a working lifetime, is the victim of a big tax bite in the most productive years. He has a further disadvantage in that his self-employed status denies him the benefits of employer-sponsored pension plans. He has a choice of trying to save enough from his earnings-after-taxes to finance retirement, or continuing to work long after his employed contemporaries are collecting pension benefits. The exclusion of the self-employed person from the benefits of OASI by his continued earnings after 65 only adds insult to injury.

The Jenkins-Keogh bills are designed to fill the needs of the self-employed, who were left out in the cold when laws were passed permitting a tax shelter for company pension plans. It should be understood that the Federal Internal Revenue Code provides substantial tax advantages to deferred compensation under so-called "approved pension plans," which is not at present matched by similar savings incentives for the self-employed. The Jenkins-Keogh bills provide that "any individual who is not eligible to participate in a pension or profit-sharing plan may set aside each year an amount not to exceed ten per cent of his earned income, and in no case more than $7,500, to be paid into a restricted retirement trust for insurance annuity. The amount thus set aside could be deducted from his taxable income. The proposed law places certain restrictions on the means by which these savings can be accumulated, and provides that the taxpayer may not tap the fund until he is sixty-five years old, except in the case of total disability."

The American Medical Association is endeavoring to arouse physicians to the advantages of this bill. The legal profession, which finds itself in the same neglected group of taxpayers as physicians, has brought this reform movement close to fruition under the leadership of the American Bar Association. The final destiny of these bills now rests with those individuals who can be counted upon to put their shoulders to the wheel at the appropriate moment. The fall recess finds most congressmen and senators at home, and this is an excellent time for all physicians to let them know of their interest in the proposal, which in amended form is now before the House Ways and Means Committee. If all goes well during the second session of the 84th Congress, it is probable that it will no longer be an economic sin for a man to work for himself.

FRANCIS H. ADLER, M.D.

A.M.A. Archives OF OPHTHALMOLOGY

The Changes in the Fundus of the Eye in Arterial Hypertension

HERMAN ELWYN, M.D., New York

The changes in the fundus of the eye which accompany arterial hypertension present two distinct pictures: (1) that due to slowly progressive changes in the retinal arteries, and without any abnormal contraction or narrowing of these arteries; (2) that in which there is seen an abnormal narrowing of the retinal arteries with secondary changes in the substance of the retina, and which constitutes arteriospastic retinopathy.

In the first picture there are seen (1) an irregular tortuosity of the retinal arteries; (2) a widening of the light reflex; (3) a hiding of a portion of the vein on each side of the artery which crosses it; (4) irregularities in the course of the arteries, and (5) occasionally, arteries which have a copper-wire or silver-wire appearance.

These elements are apt to vary considerably from a mild to a marked degree. They constitute the fundus picture seen in cases of benign essential hypertension.

In the second picture, that of arteriospastic retinopathy, there are seen (1) an abnormal narrowing of the retinal arteries; (2) hyperemia of the optic disc; (3) edema of the retina; (4) hemorrhages, and (5) cotton-wool patches. In time there are added (6) hyalin and lipid deposits in the retina, which in the area around the fovea assume a star-shaped figure.

Received for publication Oct. 31, 1955.

In this communication I shall discuss each of these fundus pictures.

THE FUNDUS OF BENIGN ESSENTIAL HYPERTENSION

The slowly progressive arterial changes which are responsible for the elements of this fundus picture are aging and arteriosclerosis. It is known since the teaching of Jores and of Aschoff that in the histological picture of arteriosclerosis the changes due to the aging process are distinct from those of arteriosclerosis proper. In the retinal arteries of the benign hypertension fundus the visible changes due to an exaggerated aging process are the tortuosity of the vessels, the widening of the light reflex, and the hiding of the vein behind the artery. The changes due to arteriosclerosis proper are the irregularities in the course of the artery. The appearance of copper-wire or silver-wire arteries is due to arteriolosclerosis.

Aging of arteries is characterized by (1) a lessening of the elasticity of the vessel walls, with the artery becoming longer and wider, and (2) a diffuse thickening of the intima. These changes occur to a moderate degree in old people, but are exaggerated in cases of long-standing hypertension. The lessening of the elasticity of the arterial walls is shown by the tortuosity of the retinal arteries and by the widening of the light reflex. The diffuse thickening of the intima cannot be seen in the course of the vessel but is shown in places where the artery

crosses a vein. Here the thickened artery hides a portion of the vein on each side of the red column.

Arteriosclerosis is characterized by a nodular thickening of the intima in an irregular distribution. The sclerotic plaques may be close together but are individually nodular. They cause irregularities in the course of the vessel. Such irregularities in the course of the retinal arteries are the only visible manifestations of arteriosclerosis there.

Arteriolosclerosis is a thickening of the small arteries and arterioles due to the subendothelial deposit of hyalin and lipids in segments of the vessels. It occurs only in cases of long-standing hypertension, and only in certain organs. It is found in the kidneys in practically every case of chronic hypertension, less frequently in the spleen and in the pancreas. It occurs also in the brain and in the retinal arteries. It is never found in the small arteries of the trunk and of the limbs. In the retina the affected arteries are apt to have a copper-wire or silver-wire appearance.

How do aging of the arteries and arteriosclerosis become exaggerated in cases of benign essential hypertension?

A. In the artery at birth there is hardly any intima. Adjacent to the media there is an elastic lamina, and this is lined by the endothelium. There is perhaps a slight amount of protoplasmic ground substance. In time a fibroelastic layer develops between the elastic lamina and the endothelium, and these layers together constitute the intima. The intima thickens during life, at first by means of elastic and collagenous fibers, after middle age mostly by means of collagenous fibers. In persons without hypertension this thickening is of a moderate degree.

When one looks for the stimulus that is responsible for the formation of the intima and for its thickening with the advancing years, one finds it in two related factors: (1) the continuous pressure on the vessel wall exerted by the blood flow in the artery and accentuated by the systole of the heart, and (2) the resistance which the arterial wall offers to the pressure exerted by the blood flow, and which causes the arterial wall to be in a certain definite state of tension.

In organs such as the kidneys, the pancreas, the spleen, and the brain, and this also holds good for the retina, the arteries regulate the flow of blood in them according to the needs of the organ. At times more blood is needed than at other times. The resistance and tension of the arterial wall to the pressure of the blood flow is therefore variable. It is this normally varying, yet continuous, resistance and tension of the arterial wall which is the stimulus to the formation of the intima, and to which the intima responds with growth. It is this continuous tension which eventually causes a lessening of the elasticity of the arterial wall.

The resistance and tension of the arterial wall in helping to regulate the normal blood flow in the artery is also the most important factor in initiating the arteriosclerotic process. With the continuous tension some of the fibers of the intima are eventually damaged in irregularly distributed areas. They are then unable to utilize the fat and other lipids which are present everywhere in the intima and which other areas are able to utilize. The unutilized fat and lipids form aggregates which become mushy, and with additional changes form arteriosclerotic plaques.

This factor of resistance and tension on the part of the arterial wall to the pressure exerted on it by the blood flow has been given a numerical value, obtained by dividing the numerical figure for the mean arterial blood pressure by the numerical figure for the blood flow as given in cubic centimeters per 100 gm. of organ per minute. Kety and his associates [2] studied the cerebral blood flow in normal young men. They found it to average 54 cc. per 100 gm. of brain per minute. Dividing the numerical figure for the mean arterial blood pressure by the numerical figure for the blood flow, they obtained a value of 1.6 for the cerebrovascular resistance.

B. In normal persons the blood enters the arteries of the organs under normal pressure. When the blood is thrown into these arteries under an increased pressure, as in essential hypertension, the organs will be flooded unless they are protected against this onrush. In spite of the increased blood pressure, the arteries maintain the normal blood flow, so that only the amount which satisfies the needs of the organ flows in its arteries. They accomplish this by the increased resistance and tension of the arterial walls. The arteries of the organs are not abnormally contracted. This is borne out by the studies of Kety. He found, in 50 cases of benign essential hypertension, that the cerebral blood flow was the same as that in normal young men, namely, 54 cc. per 100 gm. of brain per minute. He found, however, the cerebrovascular resistance increased to the numerical value of 3.0, instead of 1.6, as in the normal.

In this connection it must be understood, and the work of Kety is corroborative, that the small arteries of the brain do not participate in the maintenance of the increased blood pressure. The arteries of the brain are not abnormally contracted, as shown by the normal blood flow in them. In fact, there is no such thing as a generalized arterial contraction to maintain the blood pressure. Only the small arteries of the splanchnic circulation are abnormally contracted in benign essential hypertension. Only these vessels constitute the effector organ for the maintenance of the blood pressure under normal conditions, and they only maintain the blood pressure when it is increased.

The arteries of the kidneys in benign essential hypertension also regulate their blood flow so that it remains normal. The resistance and tension of the walls of these arteries are correspondingly increased. A similar state of normal blood flow and of increased tension of the walls of the arteries must be assumed for the retinal arteries.

In the arteries of these organs, the brain, the retina, and the kidneys, the increased resistance and tension of the arterial walls, lasting for many years in the course of benign essential hypertension, constitute the stimulus which leads to a gradual reaction on the part of the arterial walls, with (1) an exaggerated thickening of the intima, (2) a lessening of the elasticity of the arterial wall, and (3) an increased production of arteriosclerotic plaques.

In the retina these slowly progressive changes are now recognized by the tortuosity of the vessels, the widening of the light reflex, the hiding of the vein on each side of the crossing artery, and the irregularities in the course of the artery.

The increased resistance and tension on the part of the arterial wall, prolonged over years, has an added effect on the walls of some of the small arteries in the kidneys, the pancreas, the spleen, the brain, and the retina. There is a subendothelial deposit of hyalin and lipids in these small arteries, already discussed under the term arteriolosclerosis.

The factors of increased resistance and tension on the part of arterial walls in essential hypertension are of no importance in the small arteries of the striated muscles in the trunk and in the limbs. These arteries have no occasion to increase the resistance of their walls. They are always contracted when the muscles are at rest, with a minimum of blood flow in them. They dilate when the muscles are active and then are in need of an increased flow of blood. They do not participate in the maintenance of the normal blood pressure. In the absence of a proper stimulus there is, therefore, in these small arteries no abnormal thickening of the intima, no increase in the extent of arteriosclerosis, and no arteriolosclerosis.

I have so far attempted to explain the manner in which, in cases of benign essential hypertension, the slowly progressive changes of aging and of arteriosclerosis become exaggerated in the retinal arteries.

The next question is: How are the changes seen in the second fundus picture, that of arteriospastic retinopathy, brought about?

ARTERIOSPASTIC RETINOPATHY

The picture of arteriospastic retinopathy, especially as seen in young persons, is not

due to chronic progressive changes in the walls of the arteries. An acute factor characterizes this picture. There has occurred a sudden contraction or narrowing of most or all of the retinal arteries. Such a narrowing may remain for some time without being accompanied by changes in the retina. In due time, however, consequential changes are evident. As a result of the abnormal narrowing of the arteries, the terminal vessels, the capillaries, dilate, producing hyperemia. This peristatic hyperemia, so named by Ricker, is easily seen on the optic disc, which is redder than usual, and on which tiny vessels may sometimes be seen. As a result of the dilatation of the capillaries, fluid transudes through their walls, with the formation of edema in the posterior area of the retina. At a slightly later stage, the prestatic stage of Ricker, the capillary walls soften sufficiently to permit red blood corpuscles to pass through them, with the formation of hemorrhages. In some arterioles the contraction has narrowed the lumen to a degree where tiny ischemic infarcts are produced, as has been demonstrated by Friedenwald. These tiny infarcts are seen ophthalmoscopically as cotton-wool patches. They occur in the nerve fiber layer, in areas where the nerve fibers are swollen and in which cytoid bodies can be seen histologically.

When the narrowing of the arteries persists for some time, and when the substance of the retina begins to suffer from subnutrition and suboxidation, hyalin and lipids are seen irregularly scattered in the retina, and appear in the macular area as a star-figure.

Arteriospastic retinopathy varies from a mild to a severe degree, depending upon the degree of narrowing of the retinal arteries, its duration, and how the substance of the retina adapts itself to the disturbance in blood supply.

Under what conditions does an abnormal narrowing of the arteries occur, and with it the consequential retinopathy?

A. When an arteriospastic retinopathy occurs with hypertension, it is clear that there has also occurred an abnormal contraction of the small arteries of the splanchnic circulation, which is responsible for the increase in blood pressure. There are diseases in which there occurs, in addition, an abnormal contraction of the small arteries of the brain and of the kidneys. An abnormal contraction of the arteries of the brain results possibly in an anemia, or in a varying degree of edema of the brain, with severe headache, and occasionally with an attack of convulsions. Abnormal contraction of the arteries of the kidneys results in oliguria, albuminuria, hematuria, and a varying degree of renal insufficiency, with a corresponding increase in the nonprotein nitrogen of the blood.

Such a set of symptoms due to the abnormal contraction of the arteries of the brain, the retina, and the kidneys, in association with an increase in blood pressure is seen in (1) diffuse glomerulonephritis, (2) preeclampsia and eclampsia of pregnancy, (3) some of the less common forms of kidney disease, and (4) cases of pheochromocytoma.

In these diseases with different etiologies, the cause of the abnormal contraction of the small arteries in the organs mentioned is not always clear. In diffuse glomerulonephritis the spastic contraction of the arteries is possibly an allergic type of reaction following a previous infection with some organism, especially the Streptococcus. In the less common diseases of the kidneys, such as amyloid contracted kidney, periarteritis nodosa when it affects the kidneys, and polycystic kidney, it is the threat of reduction of the intraglomerular filtration pressure to which the body reacts with an increase in blood pressure and with a spastic contraction of the arteries in the organs. In cases of pheochromocytoma it is the excessive amount of epinephrine in the blood which causes the abnormal contraction of the arteries in the organs.

In preeclampsia and eclampsia of pregnancy it is the abnormal contraction of

the small arteries in the brain, the retina, the kidneys, and the splanchnic circulation that is responsible for all the symptoms. The factors which cause the abnormal arterial contraction are still not clear to most investigators. Many years ago I ventured to offer an explanation for the occurrence of the abnormal arterial contraction in preeclampsia and eclampsia of pregnancy.[1] No one has paid any attention to it. I still think that my original explanation holds true.

B. I have discussed the two fundus pictures, that of the benign essential hypertension and that of arteriospastic retinopathy as they occur separately. However, there are conditions in which one fundus picture adds itself to the other. When an acute diffuse glomerulonephritis does not heal but passes into a chronic stage, it is often accompanied by hypertension, which lasts for many years. There are now present the conditions for the development of diffuse thickening of the intima, for the lessening of the elasticity of the arterial wall, and for the development of arteriosclerosis and of arteriolosclerosis in the kidneys, the brain, and the retina. With the recurrent acute attacks the two fundus pictures combine, with the retinal arteries narrowed.

C. Of great importance is the fundus picture in cases of essential hypertension in which, after years of hypertension of a definitely benign character, there is now seen an acute arteriospastic retinopathy. The problem now is whether or not the case has entered the malignant phase, with the foreseeable fatal termination within a short time. The deciding factor is not with the fundus picture. It lies in the determination of the renal status. When there is no renal insufficiency, and no increase in the nonprotein nitrogen of the blood, the case is not one of malignant hypertension. I prefer to classify such a case as belonging to an intermediary group, distinct from the group of strictly benign essential hypertension, and from the group of cases in the stage of malignant hypertension. The cases of this intermediary group with long-standing hypertension, which now present an arteriospastic retinopathy but have normal kidney function, are the ones which, barring other factors, should respond best to such drastic treatment as sympathectomy.

MALIGNANT HYPERTENSION

The cases in the malignant stage of essential hypertension constitute a small group. In the statistic of Perera,[3] of a total of 250 cases, there were only 5 with uremia. In these cases, during a variable benign phase in which the blood pressure is very high, the resistance and tension of the walls of the arteries in the organs are necessarily very marked. The consequence is an undue thickening of the intima and an undue development of arteriosclerosis, and also of arteriolosclerosis in the small and smaller arteries of the brain and the retina, but especially of the kidneys. Eventually there occurs a loss of renal elements with diminution of renal function. There comes a time when there is added an abnormal contraction of the small arteries in the kidneys, the brain, and the retina. A vicious circle is now formed. The narrowing of the small arteries in the kidney sets the humoral mechanism in motion and aggravates the already existing spastic contraction of the arteries in the organs.

In the kidneys the now intense contraction of the small arteries causes necrosis and hemorrhage in the walls of these vessels. Renal insufficiency is now marked; the nonprotein nitrogen in the blood is increased and in most cases cannot be reduced to normal. The case has now become malignant.

In the brain the arterial contraction causes an edema of the brain, and with it an increase in intracranial pressure. There is severe headache, possibly other cerebral symptoms, and the increased intracranial pressure manifests itself by papilledema.

In the fundus of the eye there is now seen the picture of arteriospastic retinopathy added to the arterial changes of chronic hypertension, to which papilledema is frequently added.

SUMMARY

Changes in the fundus of the eye in hypertension present two distinct pictures: One is the result of exaggerated aging of the retinal arteries, of arteriosclerosis and of arteriolosclerosis, in which there is no abnormal contraction of the retinal arteries. The second picture is due to an abnormal contraction of the retinal arteries with secondary changes in the substance of the retina, and constitutes arteriospastic retinopathy.

The first picture is the one seen in essential hypertension, throughout the benign phase.

Exaggerated aging of the arteries, enhanced arteriosclerosis, and arteriolosclerosis occur in the course of essential hypertension, in addition to the retina, in such organs as the brain, the kidneys, the pancreas, and the spleen. These changes are due to the continuously increased resistance and tension on the part of the arterial walls against the pressure exerted by the blood flow in the arteries. The increased resistance and tension of the arterial walls helps maintain the normal blood flow in the organs in benign essential hypertension in spite of the increased blood pressure.

Arteriospastic retinopathy occurs with arterial hypertension, and with abnormal contraction and narrowing of the arteries in the brain and in the kidneys, in diffuse glomerulonephritis, in preeclampsia and eclampsia of pregnancy, in some of the less common diseases of the kidneys, and in cases of pheochromocytoma.

Arteriospastic retinopathy is seen in some cases of essential hypertension after years of hypertension of a definitely benign character, but without renal insufficiency. These cases constitute an intermediary group, between the group of strictly benign cases and the group in the malignant stage of hypertension.

Arteriospastic retinopathy added to the arterial changes of chronic hypertension, to which papilledema is frequently added, is seen in a small group of cases with permanent renal insufficiency. These are the cases in the malignant stage of essential hypertension.

REFERENCES

1. Elwyn, H.: A New Explanation for the Occurrence of Eclampsia in Pregnancy, Am. J. Obst. & Gynec. **10**:698, 1925.

2. Kety, S. S.: The Response of the Cerebral Blood Flow in Man to Cardiovascular Stress, in Factors Regulating Blood Pressure, Transactions of the Third Conference, May 5-6, 1949, New York, p. 262.

3. Perera, G. A.: Diagnosis and Natural History of Hypertensive Vascular Disease, Am. J. Med. **4**:416, 1948.

New Mercury Vacuum Pump and System of Slowly Applied Vacuum for Phakoerisis

ALFREDO VILLASECA, M.D., Santiago, Chile

The suction method for intracapsular cataract extraction is nowadays far less popular than the forceps method. However, a comparative study of the grasping mechanism with forceps and with the vacuum cup clearly demonstrates the superiority of the latter. In fact, the forceps "pinches" a small piece of the delicate capsule, from which the lens will hang loosely. As Thomas [1] has stated: "The entire weight of the lens and its attachments are suspended from a relatively small area." The mechanism of the grasp with a vacuum cup is quite different. When atmospheric pressure between the cup and the lens drops, the air pushes the lens against the cup, to which it adheres. Dimitry [2] has expressed this in terms physically exact when stating, "The atmospheric pressure, seeking to balance the vacuum, forces the lens into the cup."

The advantages of this grasp are the following: 1. There is no pinching of the capsule, but adhesion to the erisiphake takes place, owing to the normal atmospheric pressure from outside. 2. If the zonule is very strong, the cup may slip and release the grasp (reapplication is again possible) as an alternative to tearing the capsule, which is bound to happen with a strong forceps pull that has no such escape-valve mechanism. 3. Due to the larger surface of contact of the erisiphake, the traction lines in the capsule have greater uniformity of distribution.

The percentage of ruptured capsules will naturally be less with a suction cup than with forceps. The statistics of various authors corroborate this. Castroviejo [3] experienced 20% to 30% of ruptured capsules with the forceps (he used Verhoeff's forceps at that time) and less than 10% with the cup. Moreu [4] contends to a very poor statistic of intracapsular extractions with forceps, contrasting with 94% of total extractions with the erisiphake. In 537 operations with forceps, Thomas [1] experienced 87 capsular ruptures, that is, 16.2%, while in 75 operations with suction there was not one case of tearing of the capsule.

Why is it, then, that erisiphake extraction is not as popular as forceps extraction? There are, in my opinion, two reasons: (1) There is no perfect or ideal apparatus to generate and apply vacuum, and (2) Barraquer's * original idea of applying vacuum "suddenly" (to obtain instantaneous zonulotomy) has been resisted by ophthalmologists, who consider it dangerous. There is the fear of a sudden sucking of vitreous if the cup is improperly placed, surpassing the equator of the lens, or of tearing the root of the iris should this be pinched by the rim of the erisiphake.

The purpose of this paper is to do away with these objections by (1) introducing a new vacuum generator, based on the simple displacement of mercury between two bottles, and (2) advising the use of a "progressive"

Accepted for publication Sept. 19, 1955.

From the Department of Ophthalmology, Hospital Salvador.

* References 5 and 6.

vacuum, provided by this apparatus, as opposed to Barraquer's instantaneous vacuum.

The following points will be considered:

1. The physics of a vacuum
2. Vacuum generators used at present in cataract extractions
3. New mercury vacuum pump (vacuogener)
4. Physical conditions of the erisiphakes
5. System of slowly applied vacuum, as against instantaneous sucking

THE PHYSICS OF A VACUUM

A vacuum is the absence of air and therefore of atmospheric pressure. A vacuum cup acts by the more or less complete extraction of air existing between its surface of contact

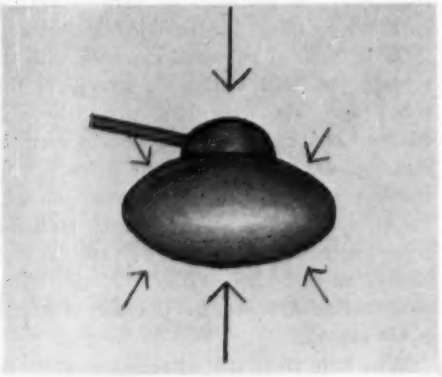


Figure 1

and the object on which it is applied. Thus, atmospheric pressure at the outer surface of the cup and in the rest of the object not covered by the cup pushes the object against the cup and vice versa (Fig. 1).

It is important to understand that vacuum itself is only the lack of air, and not an active force. The power is represented by atmospheric pressure existing in its immediate surroundings.

The weight of the column of air 300 km. high, which forms the atmosphere, can be indirectly measured, as it is neutralized by a column of mercury 76 cm. high at sea level (Torricelli's experiment), and with a column of 10.33 meters of water (discovery of atmospheric pressure in the Toscana wells in the 17th century).

As the weight of a column of water 10.33 meters high is 1 kg. and 33 gm. per square centimeter of surface, this is also the weight of the atmosphere at the surface of the earth (atmospheric pressure). The pressure exercised on a square meter is 10,330 kg., and it is calculated that the pressure brought to bear by the atmosphere on the body of a man of medium height is equivalent to a weight of 16,000 kg. As this pressure is exercised both from the outside inward and from the inside outward, it is not felt.

One of the principles of physics which is applied in all vacuum generators is Mariotte's Law. This can be expressed thus: The volume occupied by a mass of gas is inversely proportional to its pressure. This means that if 1 liter of air with a normal atmospheric presure of 76 cm. Hg is placed in a container double its volume (2 liters), gas pressure will drop to one-half (38 cm. Hg). If, on the other hand, this mass of air is compressed into the space of 0.5 liter, its pressure will increase to double (152 cm. Hg). That is, the product of the volume of the gaseous mass by its pressure is a constant.

In the various devices where a vacuum is generated, air is expanded by different mechanisms in order to decrease its pressure (rotary pumps with vanes, syringe plungers, rubber bulbs, etc.).

Naturally, the vacuum which can be produced with any apparatus has a maximum which cannot be exceeded and which is equivalent to the atmospheric pressure existing in that locality. When air is completely eliminated at a surface (absolute vacuum), the surrounding atmospheric pressure acts without counterweight (maximum of 76 cm. Hg at sea level).

VACUUM GENERATORS USED AT PRESENT IN CATARACT EXTRACTION

There are at present two types of instruments used to produce a vacuum: (1) rotary pumps driven by electric motors (models of Barraquer, Castroviejo, Nugent, Berliner, etc.) and (2) syringes or rubber bulbs for manual use (models by Arruga, Dimitry[7] Perez Llorca,[8] Bell,[9] Harrington,[10] etc.).

The rotary pumps consist of a cylindrical container which is partially occupied by a revolving cylinder eccentrically placed (Fig. 2). The cylinder has longitudinal grooves in which vanes are inserted loosely. In spite of the eccentricity of the revolving cylinder, vanes are always in close contact with the wall of the container, as they are forced out of the cylinder grooves. When the cylinder revolves at great speed, impelled by an electric motor, there is an expansion of air (vacuum) behind the revolving vanes and compression (pressure) in front of them. There are, of course, a suction and a pressure tube.

The disadavantages of motor suction, as repeatedly pointed out by various authors, are as follows: 1. Mechanical disabilities: jamming of the pump; electrical flaws. A sudden loss of vacuum can be dangerous if it happens when the lens is already free from all zonular attachments. 2. Necessity for constant care (cleaning and oiling). 3. High price. 4. Instantaneous suction. 5. Continuing aspiration if the erisiphake loosens its grasp.

On the other hand, the advantage of motor suction is that it is possible to obtain a high vacuum of known value (measured with a vacuometer connected to the suction tube).

The disadvantages of suction with syringes or rubber bulbs are as follows: 1. The vacuum cannot be measured or graduated, as there is no vacuometer. 2. As the vacuum chamber is very small, the slightest misplacement of the cup on the capsule will produce an air bubble inside the syringe or rubber bulb, which will decrease (by an unknown amount) the degree of its vacuum. 3. A greater number of hand movements is required to generate a vacuum.

Figure 2

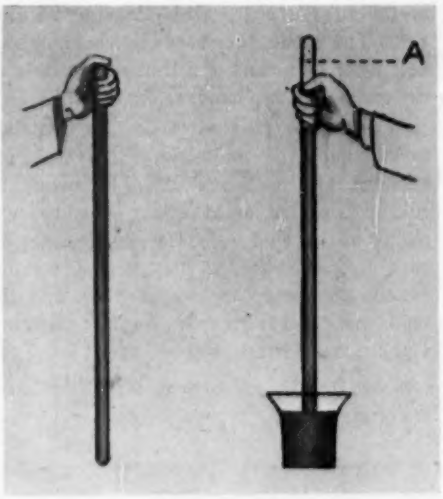


Figure 3

On the other hand, they have the following advantages when compared with motor suction apparatus: 1. The cost is low. 2. Little maintenance care is required. 3. They are less dangerous, as they produce a slowly increasing vacuum (valves have been eliminated in practically all up-to-date models). 4. When the grasp is loosened, the vacuum is automatically interrupted.

Other types of vacuum generators which have been used in cataract extractions are water spouts (Marbaix [11]), oral suction (Falcão [12]), steam condensation (Muñoz Urra [13]), and the rarefaction of air in a container by means of an inhaling pump (Hulen,[14] Lagrange,[15] O'Reilly and Grant [16]). These methods have not had many followers, owing to obvious disadvantages.

NEW MERCURY VACUUM PUMP (VACUOGENER)

This apparatus is based on Torricelli's well-known experiment, which gave birth to the barometer (Fig. 3).

Over the mercury column, which annuls the weight of the atmosphere, there remains

in the tube a space with absolute vacuum (*A*). The vacuogener uses this vacuum, connecting it by means of a thin rubber hose to the erisiphake applied over the lens (Fig. 4).

By applying Mariotte's Law, it is simple to calculate the intensity of the resulting vacuum. The small quantity of air inside the rubber hose (of atmospheric pressure) expands in the void (*A*), decreasing its pressure in proportion to its greater volume. Should the hose capacity be 5 cc. and the void space (*A*) over the level of mercury 150 cc., the formula will be:

76 cm. Hg×5 cc.=*X*×150 cc. $X=\frac{76\times5}{150}=2.5$ cm. Hg of gas tension

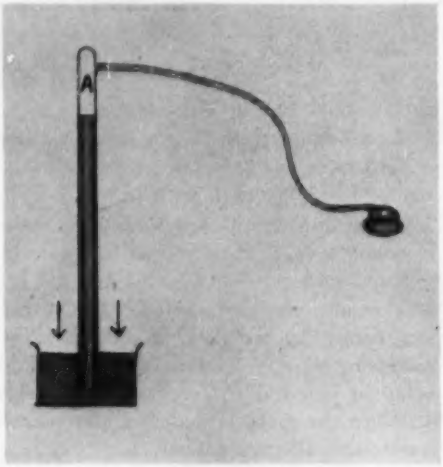


Figure 4

This is equal to a negative pressure (vacuum) of 76 —2.5—73.5 cm. Hg.

The vacuogener essentially consists of two Pyrex bottles (*A* and *B*) and a glass tube or plastic hose (*C*) connecting them (Fig. 5). The hose is 76 cm. long, the length of the barometric column of mercury at sea level. The bottles *A* and *B* are of the same diameter, but the second one is taller. Bottles and hose are fixed in a rectangular base, which rotates around the fixed axis *D*, normal to the drawing.

In position *1* (Fig. 5) the two bottles are in communication with the atmosphere, and mercury naturally reaches the same level in them. A line joining the two mercury levels in this horizontal position should cut the axis of rotation *D*.

On tilting the apparatus to the left to position *2* (Fig. 6), there is a displacement of mercury toward bottle *A* until it is filled completely, thereby expelling all the air from this bottle. The level of mercury rises slightly in tube *1* and is detained by stopper *2*. The thin rubber hose, *E* (sterile), is then joined to tube *3* of the vacuogener by one side (nurse) and to the erisiphake (*F*) by the other side (surgeon). When the erisiphake is fitted into the rubber hose, it is important to take care that the cup remains in a downward position in order to avoid having to rotate the hose during the application.

With the vacuogener in this position (Fig. 6), in which no vacuum is yet produced, owing to its communication with the atmosphere, the cup is gently placed over the anterior surface of the lens. This closes the only communication of the atmosphere with bottle *A*.

On the other hand, bottle *B* is always in communication with the atmosphere through tube *4*.

The nurse now rotates the vacuogener to the right, and the mercury gradually passes in bottle *B*. The small amount of air contained inside the thin hose *E* expands into the space left void in bottle *A* by the displacement of mercury (Figs. 7, 8, and 9), thus generating an increasing vacuum, in accordance with Mariotte's Law. The apparatus has an axis of adjustable friction, and it remains therefore fixed at any desired position.

With a volume of 160 cc. for bottle *A* and a hose *E* with a section of 2.5 mm. and 150 cm. long, the maximum vacuum produced in the vertical position (Fig. 9) has been 65.5 cm. Hg in Santiago, Chile (500 meters above sea level, atmospheric pressure 71.5 cm. Hg). At sea level the maximum vacuum will be somewhat greater (about 70 cc. Hg).

Inside the bottle *B* a glass tube (*5*) hinders the admittance of air into hose *C* and bottle *A* in the vertical position (Fig. 9).

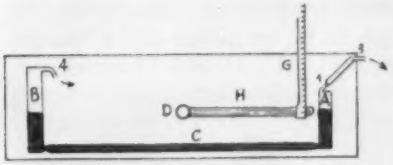


FIG. 5

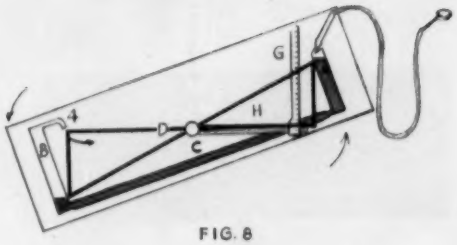


FIG. 8

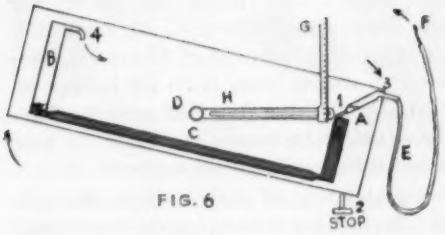


FIG. 6

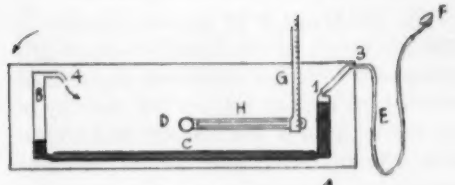


FIG. 7

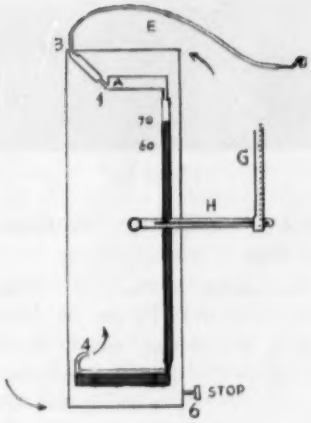


FIG. 9

Figures 5-9

Mercury levels in bottles *A* and *B* in the intermediate positions of the apparatus (Figs. 6, 7, and 8) and in hose *C* in the vertical position (Fig. 9) permit a direct reading of the degree of vacuum.

In the intermediate positions (Figs. 6 to 8) the reading is taken on a graduated scale (*G*), which originates at the horizontal bar (*H*) attached to the fixed axis *D*. The height of mercury level in bottle *A* above the horizontal bar (*H*) is equal to the lowering of mercury level in bottle *B* below the same bar (*H*), as the two bottles are of the same diameter and equidistant from axis *D*. This is geometrically proved by the equating triangles drawn in Figure 8. As mentioned before, the mercury levels in the initial horizontal position (Fig. 5), with both bottles in communication with the atmosphere, must be in the same line with the axis of rotation, *D*. Thus, the scale *G* (graduated as a duplicate of an ordinary centimeter scale) measures directly the distance between the mercury levels in bottles *A* and *B*.

In the vertical position, wherein the higher level of mercury is outside bottle *A* (Fig. 9), the reading of the degree of vacuum can be made on an ordinary centimeter scale beside hose *C*. In practice, it is only necessary to

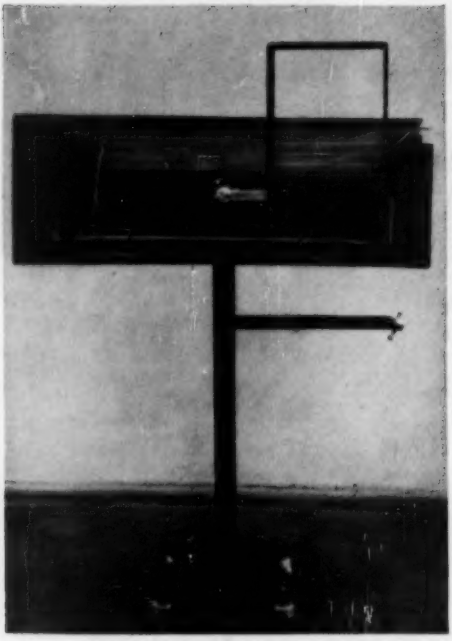


Figure 10

use scale *G*, where pressure can be read up to 65 cm. Hg.

The vacuogener is therefore a vacuum generator (from 0 to 70 cm. of mercury), and also a vacuometer which simultaneously measures the degree of vacuum produced. The photographs in Figures 10 to 14 show the vacuogener at work. The lens is represented by the rubber balloon filled with water placed on the platen of the balance. Figures 10, 11, 12, 13, and 14 correspond, respectively, to the schemes represented in Figures 5, 6, 7, 8, and 9. The vacuogener is placed at the side of the eye not operated on, with its axis of rotation opposite the patient's head. At the rear of the apparatus (Fig. 15) there is a quadrant numbered from 1 to 6 (corresponding to vacuums from 10 to 60 cm. Hg), which permits the nurse to follow the surgeon's orders from behind without having to look at the mercury column. On tilting the vacuogener until the arrow is in front of, say, number 4, it will generate a vacuum of 40 cm. Hg, provided, of course, there is no air leakage on the erisiphake being applied over the lens. The plastic tube shown in Figure 15 connects bottle *B* with the atmosphere.

A modification of the same apparatus consists in replacing the rectangular rotary base with fixed bottles by a fixed support with vertically moving bottles. The bottles now move in opposite directions on two toothed bars, as in a pneumothorax apparatus.

The disadvantage of this modification is that the weight of the mercury column falls unsupported on the suspended plastic hose which joins the two bottles. The mobility of the bottles affords less stability and protection than in the rotating model described above.

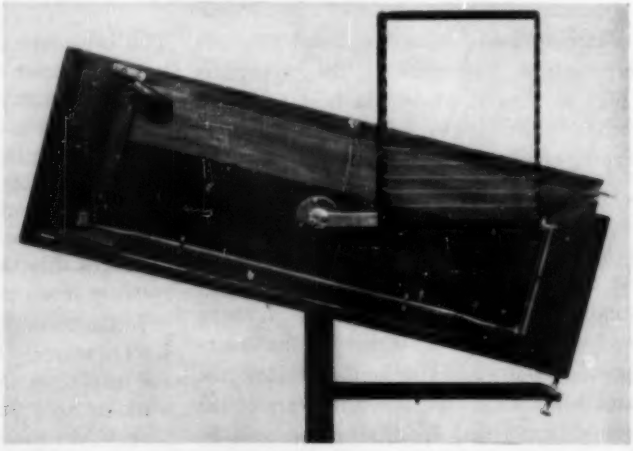


Figure 11

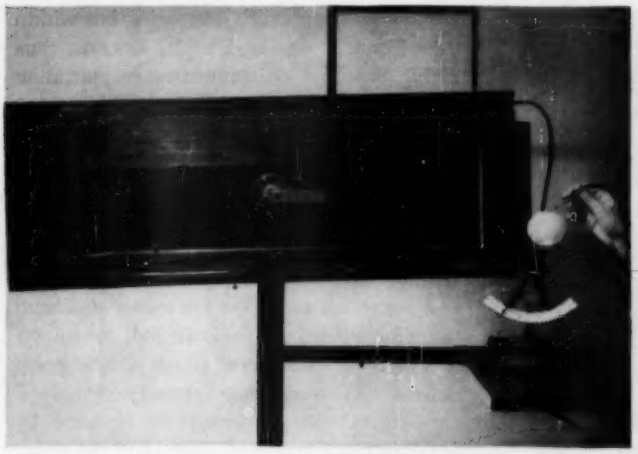


Figure 12

The vacuogener is free of the disadvantages mentioned above, both for the motor suction apparatus and for the syringe or rubber bulbs. It has, in fact, the following advantages: 1. It is free of mechanical faults, due to its simple working principle of displacement of mercury between two bottles. 2. It requires little maintenance care. 3. It provides any vacuum intensity from 1 to nearly 70 cm. Hg, gently and noiselessly. 4. It has no air valves. 5. Slowly increasing suction can be used, thus avoiding the danger of abrupt sucking. It is also possible to apply an instantaneous vacuum, as in Barraquer's technique, by placing a mosquito forceps or an air valve in the distal end of hose *E*. 6. An exact measurement of the degree of vacuum is indicated by the height of mercury levels within the apparatus itself (a perfect vacuometer, as opposed to the somewhat erratic gauge indicators commonly used). 7. The steady position of the mercury column is a valuable index to indicate whether the grasp is good. If the erisiphake has not been properly applied, air will leak inward and the mercury level will go down. If the cup adheres correctly throughout the lens surface, the mercury will remain set at a given level (10 or 20 cm. Hg). Having thus ascertained that the grasp is

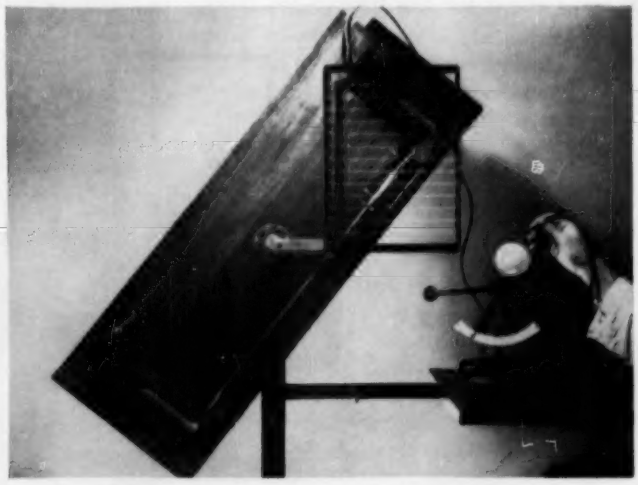


Figure 13

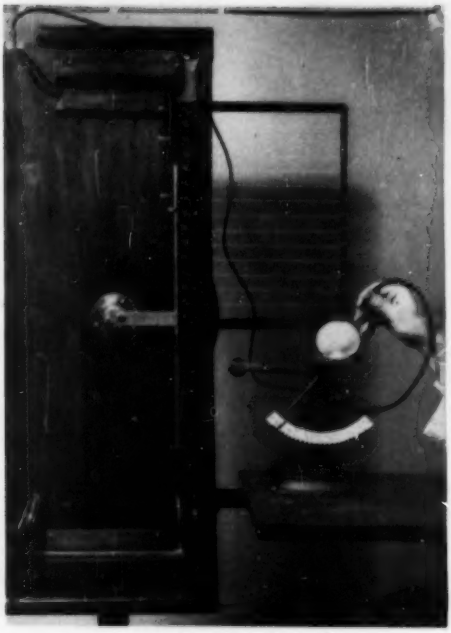


Figure 14

correct, one can then rotate the apparatus farther to the right to produce higher vacuum intensities without danger. 8. The vacuum is reversible. Should it be realized, for example, that the iris has been pinched by the rim of the cup, it would be enough to rotate the vacuogener toward the left to cancel the vacuum. 9. There is a limited vacuum reserve in bottle *A*. If the cup releases the grasp, sucking will continue (decreasing but within useful limits) during 5 to 10 seconds, thus giving time for an immediate reapplication of the erisiphake. If there has been too great a drop in the intensity of the vacuum, it will be necessary to place the vacuogener again in the initial position, until all the air has been expelled, and then make a new application. To avoid loss of the vacuum chamber *A*, when the cup loosens the grasp, at a surgeon's order the nurse can also bend the hose *E* in its proximal end, to cut off sucking. This maneuver allows a new grasp with a loss of vacuum intensity of only 7 cm. Hg, which can easily be replaced by rotating the vacuogener slightly to the right.

PHYSICAL CONDITIONS OF THE ERISIPHAKES

It is easy to understand the fundamental importance of the instrument with which a vacuum will be applied over the lens, as the force of the vacuum (atmospheric pressure) is proportional to the surface it covers (1 kg. per square centimeter). The intensity of the vacuum used is important only in correlation with the active surface of the erisiphake. A vacuum of high intensity will produce a slight suction force if the surface of the cup is small, and vice versa.

It is possible to calculate mathematically the active surface of an erisiphake, considering the diameter and depth of its cup. In a

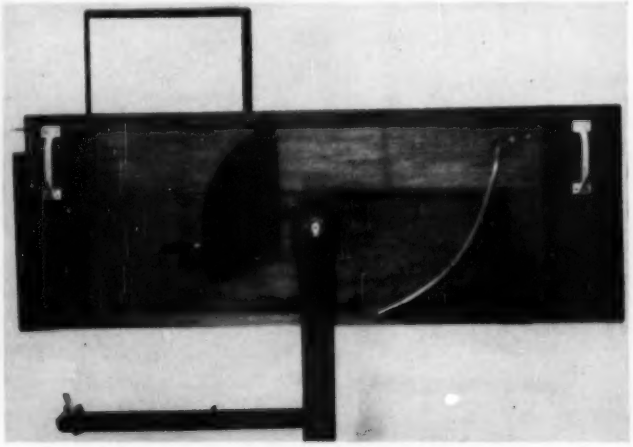


Figure 15

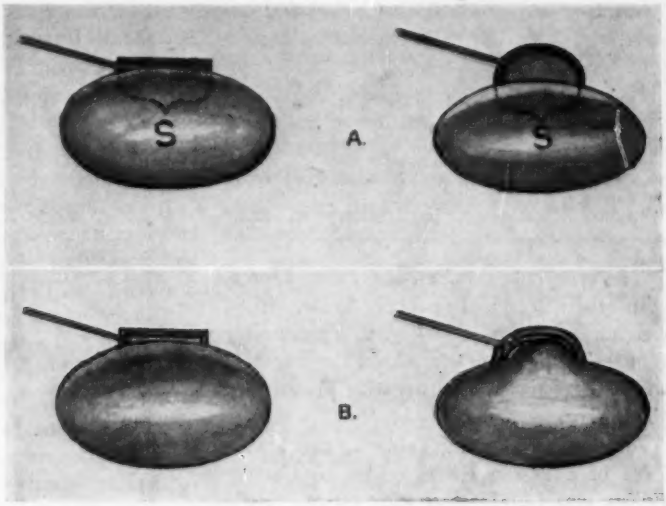


Figure 16

circular cup with an ideally level surface the calculation is based on the formula πr^2. Should the surface of the cup be hemispherical, the formula would be $2\pi r^2$ (surface of a sphere$=4\pi r^2$).

The consistency of the body on which the suction is applied is also important. Should the body be rigid, the force of suction will be the same whether a level or a hemispherical cup of equal diameter is used, as the body surface on which the vacuum acts is the same (Fig. 16*A*). On the other hand, if the body is soft and tends to mold within the cup, maintaining close contact with its inner surface, the active surface, and therefore the sucking force, will be twice as much in a hemispherical cup as in a level one of equal diameter (Fig. 16*B*).

Figure 17

With a method similar to that used by Falcão [12] it is possible to measure in grams the force of adhesion of a vacuum cup. A rubber balloon filled with water is placed on a mail balance (Fig. 17). The nozzle of the erisiphake is adjusted to the balloon, a vacuum is created, and the cup is drawn slowly and progressively away from the platen of the balance, noting the decrease of the weight in grams, at the precise moment of its liberation.

In our experiments we have used a water-filled balloon weighing 190 gm. The balloon must be soft and not tense, so as to allow a better adhesion to the rim of the cup. Traction must be effected strictly perpendicular to the surface of contact.

Different types of cups were connected with the vacuogener, and the force of adhesion with 40 and with 60 cm. Hg is shown in Table 1.

TABLE 1.—*Force of Adhesion with Various Types of Cups*

Cup	40 Cm. Hg	60 Cm. Hg
Dimitry	25	45
Bell	20-25	45
Castroviejo	..	20-25
Falcão	20	60
Perez Llorca	30	90
Barraquer	55	105
Author	45	70

The erisiphakes of Bell and Perez Llorca, with their original rubber bulbs, lifted weights of 20 and 30 gm., respectively (squeezing them tightly within the fingers), which corresponds to a negative pressure of 40 cm. Hg.

As can be seen in Table 1, the lowest force of adhesion corresponded to Castroviejo's cup (20-25 gm. with 60 cm. Hg), which has the smallest diameter (2.8 mm.), and the highest force, to that of Barraquer (105 gm.), with the largest cup diameter (4.1 mm.). When connected to the vacuogener, Barraquer's erisiphake lifted 20 gm. with a pressure of 30 cm. Hg, that is to say, the same weight as that Castroviejo's cup could lift with 60 cm. Hg. Thus, the vacuum intensity is not per se an index of the force of suction used and must always be correlated with the model of cup being employed.

With the same negative pressure of 60 cm. Hg, the cups of Falcão, Perez Llorca, and Barraquer and my own lift practically double the weight of those of Dimitry, Bell, and Castroviejo (Table 1).

Measurements of the erisiphake cups used in the previous experiment gave the results shown in Table 2.

The external size of the same erisiphakes are shown in Table 3.

TABLE 2.—*Measurements of Various Erisiphake Cups*

	Diameter of Nozzle, Mm.	Depth, Mm.
Dimitry	3.2	0.9
Bell	3.1	0.8
Castroviejo	2.8	1.3
Falcão	3.4	1.35
Perez Llorca	3.5	1.8
Barraquer	4.1	1.9
Author	4.0	1.2

Of the last four cups, with greatest sucking force, Barraquer's and Perez Llorca's have a high cup (2.25 and 2.3 mm.) and a rather bulky appearance, while that of Falcão and my own are both thin (1.8 and 1.6 mm. high) and delicate, like those of Dimitry, Bell, and Castroviejo (Fig. 18).

It can also be seen in Table 3 that the external diameter of the erisiphakes shows less variation: 4.6 to 5.7 mm. (average, 5 mm.) (Fig. 19).

The difference between the external diameter (Table 3) and the cup nozzle (Table 2) varies from 1.9 to 1.2 mm. in the different models studied. The reason for this is that in most erisiphakes the rim of the cup has a ring or collar of variable width, which reduces its opening (Fig. 20, *r*). The purpose of this ring is to prevent the lens capsule from obstructing the opening of the tube (laterally placed) before the extraction of all the air in the cup has been completed.

TABLE 3.—*External Measurements of Erisiphakes*

	External Diameter, Mm.	Total Height, Mm.
Dimitry	5.1	1.75
Bell	4.6	1.6
Castroviejo	4.7	1.8
Falcão	4.6	1.8
Perez Llorca	5.4	2.3
Barraquer	5.7	2.25
Author	5.0	1.6

In my model this ring has been abolished so as to take advantage of the whole active surface in the cup. To this end we have transferred the opening of the tube to the highest point in the cup, which is the last to be filled by the lens (Fig. 21).

In this manner we have obtained an ample opening of the cup (4 mm.), greater than those of the other models of erisiphakes, with the exception of Barraquer's (Table 2). At the same time, the external diameter is not larger (5 mm.).

It has also been considered convenient not to increase too much the depth of the cup (Table 2) in order to avoid an exaggerated expansion and bursting of the capsule. In my cup a tight contact is maintained between its inner surface and the lens cap-

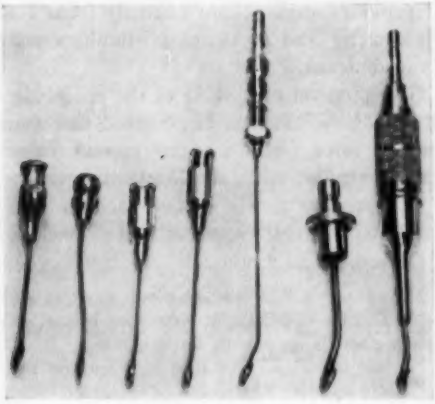


Figure 18

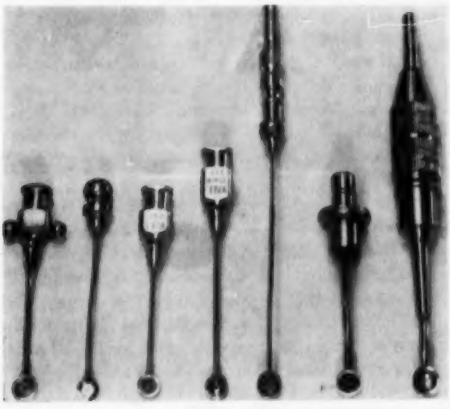


Figure 19

sule (Fig. 21) in order to hinder capsular expansion and diminish the risk of its rupture. The other models of erisiphakes, with rings that reduce their nozzles, maintain a void hoop in which the lens is not restrained by the wall of the cup (Fig. 20, *o*). On the other hand, the collar has the advantage of avoiding in part the sliding of the cup over the lens.

Falcão's erisiphake shows only a narrow ring, having thus also a small difference between its external diameter and the opening of the cup (1.2 mm.). Its depth and inner curvature are quite similar to those of my model.

The vacuogener can be used with any type of erisiphake. When doing so, it will be necessary to consider their different suction forces (Table 1) to decide on the most appropriate vacuum intensity.

SYSTEM OF PROGRESSIVE VACUUM AS OPPOSED TO INSTANTANEOUS SUCKING

Barraquer † considered that the erisiphake was superior to the forceps in that it worked both as a pneumatic forceps and as a zonulotome. He further insisted on the need for applying instantaneous vacuum to produce a sudden rupture of the zonular fibers at their lens insertion, without giving time for the

† References 5 and 6.

Figure 20

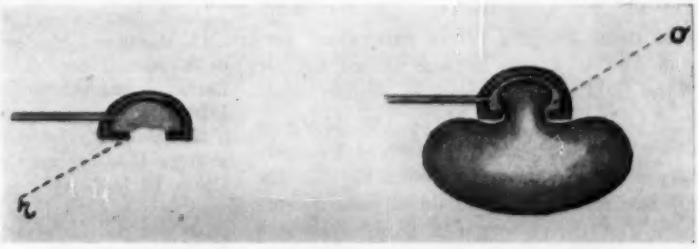


Figure 21

force to be transmitted to their peripheral end, thus preventing ciliary hemorrhages and inflammation.

It was proved thereafter that when the lens is delivered with intracapsular forceps the zonular fibers always separate at the lens insertion, this being their most fragile spot. Furthermore, the need for applying traction or doing tumbling maneuvers with the erisiphake shows that in most cases the zonule does not break with the application of instantaneous vacuum.

We must therefore consider the erisiphake only as an ideal pneumatic forceps. The moderate reduction of the equatorial diameter of the lens places the zonular fibers under slight tension and favors their subsequent rupture with traction and pressure maneuvers.

It is our contention that the system of using instantaneous sucking should be abandoned, as it has no practical purpose and might be dangerous if the cup is improperly placed (vitreous aspiration, tearing of the root of the iris). Instantaneous vacuum will also increase the possibility of capsular rupture.

The risk of capsular ruptures may be also diminished by using erisiphakes that prevent the expansion of the lens within their cups (not too deep and without anfractuosities).

With the vacuogener it is possible to apply a slowly increasing vacuum. The cup is applied over the lens before generating suction. The apparatus is then rotated slightly to the right to produce a low vacuum intensity (10 or 20 cm. Hg). The grasp is checked by the steady position of the mercury column at this level, indicating that the cup is correctly adherent throughout its surface. The vacuogener can then be rotated farther to the right to produce higher vacuum intensities.

SUMMARY

A new vacuum generator (named vacuogener) is presented. It is based on the simple displacement of mercury between two bottles. The advantages of this apparatus are analyzed, as compared with motor-driven rotary pumps and syringes or rubber bulbs. It provides any vacuum intensity from 1 to 70 cm. Hg and measures it simultaneously (vacuometer).

The physical conditions of the erisiphakes are analyzed and it is emphasized that their suction force (with a given vacuum intensity) depends mainly on their active surface.

A system of slowly applied vacuum is advised, as opposed to instantaneous sucking.

Marcel Duhaut # 2959.

REFERENCES

1. Thomas, C.: Cataract Extraction by the Suction Method, Arch. Ophth. **39**:805, 1948.

2. Dimitry, T. J.: Evolution of a Sucking Disk for Intracapsular Extraction of Cataract, Arch. Ophth. **21**:261, 1939.

3. Castroviejo, R.: Theoretical and Practical Study of the Intracapsular Cataract Operation, Am. J. Ophth. **15**:406, 1932.

4. Moreu, A.: Notas relativas a la extracción intracapsular del cristalino, in Estudios e informaciones oftalmológicas, Instituto Barraquer, 1949, Vol. 1, No. 14.

5. Barraquer, I.: Sur la Phakoérisis, Ann. ocul. **157**:702, 1920.

6. Barraquer, I.: Intracapsular Method of Cataract Extraction, Brit. M. J. **2**:660, 1924.

7. Dimitry, T. J.: A Vacuum Grasping Instrument for Removal of Cataract in Capsule, Arch. Ophth. **9**:261, 1933.

8. Perez Llorca, J.: Simplicación del procedimiento del vacío para la extracción de la catarata senil, Arch. Soc. oftal. hispano-am. **7**:384, 1947.

9. Bell, A.: A Modified Erisophake, Am. J. Ophth. **31**:610, 1948.

10. Harrington, D.: A New and Simplified Erisophake, Am. J. Ophth. **34**:435, 1951.

11. Marbaix: Réflexions sur trois cas d'extraction de la cataracte dans sa capsule par la ventouse de Barraquer sans vide vibratoire, Ann. ocul. **158**:801, 1921.

12. Falcão, P.: Technique of Cataract Operation with the Oral Suction Cupping Apparatus, Am. J. Ophth. **30**:1428, 1947.

13. Muñoz Urra, F.: Un Moyen simple pour la production du vide nécessaire pour l'extraction de la cataracte "in toto" selon la méthode de Barraquer (phacoérisis), Ann. ocul. **158**:809, 1921.

14. Hulen, V. H.: Vacuum Fixation of the Lens and Flap Suture in the Extraction of a Cataract in Its Capsule, J. A. M. A. **57**:188, 1911.

15. Lagrange, H.: L'extraction pneumatique du cristallin par rupture zonulaire, Ann. ocul. **174**: 387, 1937.

16. O'Reilly, G., and Grant, G.: La Extracción neumática de la catarata, Arch. chilen. oftal. **10**: 125, 1953.

Epidermoid Carcinoma of the Lacrimal Sac

ROBERT J. DAVIS, M.D., Iowa City

Both benign and malignant tumors of the lacrimal sac are uncommon. Prior to 1938 Penman and Wolff [1] were able to find only 64 cases of lacrimal sac tumor described and reported in the world literature. Ashton, Choyce, and Fison [2] have stated that there were 73 such tumors reported up until 1950. In 1952 Duke-Elder [3] described an additional 60 cases of tumor of the lacrimal sac. However, 26 of these were granulomas. When these 26 cases are disregarded, the total number of cases of true neoplasms of the lacrimal sac is now in excess of 100.

It appears that epithelial tumors are slightly commoner than nonepithelial tumors. It is probable that the diagnoses of "carcinoma," "malignant papilloma," and "epithelioma" represent different stages of cylindrical-cell carcinoma and that such tumors form about 50% of all reported cases.

In most cases of lacrimal sac tumor described in the literature the neoplasm has been of the invasive or infiltrative type. Epithelioma of the nasolacrimal sac of the columnar type has been reported as carcinoma in situ; rarely, secondary carcinoma of the nasolacrimal sac is discussed. A single, but extremely interesting, case was described by Locke.[4] This tumor developed secondarily to Bowen's intraepithelial epithelioma of the bulbar conjunctiva. After five years the disease reached the sac and became malignant. It took on the characteristics of a relatively undifferentiated squamous-cell carcinoma.

From the pathological point of view, it is of interest and importance to note that exactly similar tumors arise from the respiratory epithelium in the nasal and in the paranasal cavities. This similarity is important, because the nasal tumors, although uncommon, are less rare than the corresponding growths in the lacrimal sac. Therefore, they are more accessible for study.

The normal lining of the lacrimal sac is composed of cylindrical cells. Repeated irritation, due to chronic inflammation, may cause this membrane to become thickened and to form several layers of cells, which change to the squamous variety. Consequently, sections may show the cylindrical-, transitional-, or squamous-cell type.

It is probable that the primary epithelial growths of the lacrimal sac are all of the same nature. Although they may appear benign histologically, they possess malignant potentialities of varying degree, and there is a strong tendency toward recurrence. Therefore, it is clear that all nasal polyps and lacrimal tumors should be subjected to careful histological examination, even though the clinical findings do not suggest malignancy.

REPORT OF A CASE

The case forming the basis for this report is that of a 39-year-old man, who apparently had been well until seven months prior to admission. At this time he first noted a swelling along the right side of his nose near the eye. The swelling was neither painful nor tender. It gradually increased in size and caused trouble only in that it was irritated by the nosepiece of the patient's glasses. In addition, he had noted epiphora, of four or five months' duration.

The patient's past history and family history were noncontributory. The only positive physical finding related to the eye was a hard, fixed mass slightly nasal and inferior to the right internal canthus, measuring 0.5 by 1 cm., which was nontender and not inflamed (Fig. 1). Both eyes were otherwise normal in all respects. Further examination of the mass revealed that it could not be expressed and that the right lacrimal duct was irrigated with difficulty. It seemed that part of the tumor emptied

Received for publication Oct. 28, 1955.

From the Veterans Administration Hospital and the Department of Ophthalmology, State University of Iowa.

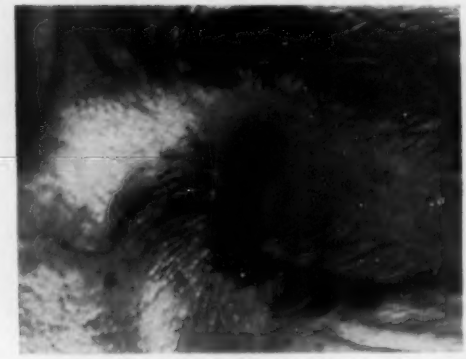


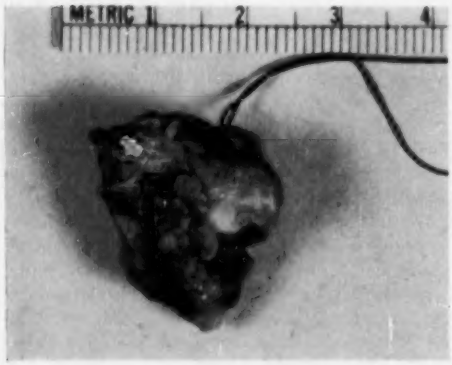
Fig. 1.—External appearance of the tumor.

into the nose, but the mass did not become appreciably smaller.

Although initial x-rays of the orbit were reported as normal, the suspicious nature of the lesion demanded that it be investigated. Hence, the mass was excised with the patient under general anesthesia (Fig. 2). At the time of operation, on Sept. 30, 1954, there was little difficulty in identifying the mass, and a clean dissection was accomplished around it. However, at the base of the tumor it seemed more firmly fixed to the underlying tissues, and there were several tiny bone fragments attached to the mass following its extirpation. These were assumed to be part of the nasal bone, where the tumor had attached. Subsequently, this proved to be true; the pathological diagnosis was epidermoid carcinoma, well differentiated, of the right lacrimal sac (Fig. 3).

The postoperative course was uneventful. In view of the pathological report, it was recommended that the patient undergo an external frontal approach to the ethmoid cells, with complete exenteration of the ethmoid cells down to the sphenoid. It was hoped that in this manner the tumor would be completely excised. The operation was performed three weeks later, on Oct. 26. The patient tolerated the procedure well, and again the postoperative course was without complication except for a draining sinus of short duration, which caused secondary conjunctivitis. The histological examination of the excised tissue and tissue borders showed no evidence of malignant cells. During the postoperative follow-up period there was discovered a submental lump, which was suspected to be a lymph node that had become involved with metastases. A submental lymph node dissection was done on Dec. 22, 1954; the pathological report showed no metastases.

Fig. 2.—The tumor after excision.



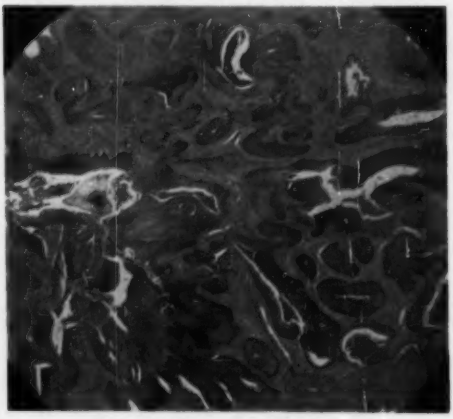


Fig. 3.—Microscopic appearance of epidermoid carcinoma.

At the time of this report the patient's condition is satisfactory. He is being followed as an outpatient.

REFERENCES

1. Penman, G. G., and Wolff, E.: Primary Tumors of the Lacrimal Sac, Lancet **1**:1325, 1938.

2. Ashton, N.; Choyce, D. P., and Fison, L. G.: Carcinoma of the Lacrimal Sac, Brit. J. Ophth. **35**:366, 1951.

3. Duke-Elder, S.: Tumors of the Lacrimal Sac, in Text-Book of Ophthalmology, Vol. V, St. Louis, C. V. Mosby Company, 1952, p. 5345.

4. Locke, J. C.: Primary Carcinoma of the Nasolacrimal Sac, Arch. Ophth. **46**:229, 1951.

Spear Cataract

LT. CHARLES O. PARKER Jr. (MC), U.S.N.

Vogt,[1] in 1922, described an unusual type of congenital cataract with crystal formation under the name of "spear cataract." His patient was a 9-year-old child with bilateral lens changes. These changes consisted of many shiny crystalline needles projecting in various directions throughout the axial area of the lens, being grouped around denser central opacities and having no apparent relation to the anatomic structure of the lens. Some areas resembled a spiny plant; others resembled a caterpillar. Some of the crystals were iridescent; some were over a millimeter in length and were grouped in bundles resembling tyrosine crystals. One lens was extracted and subjected to chemical analysis, which showed a predominance of cystine.

Three years after this case was published, Romer * investigated the remainder of this family and discovered a marked tendency toward cataract formation. Out of 42 persons, in four generations, he found 10 with what appeared to be spear cataract. Romer and Vogt were able to examine five of these and noted a marked similarity of all cases. They concluded that this condition was a dominant familial characteristic.

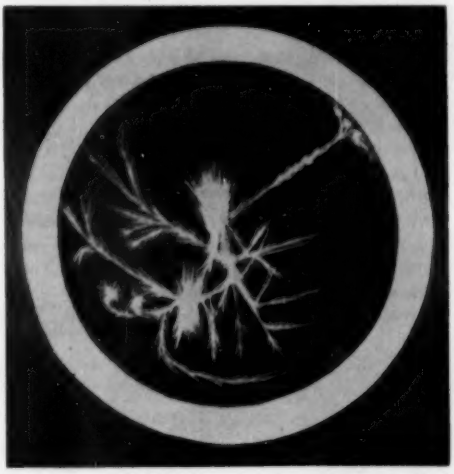
Renard and Laporte,[3] in 1951, made a thorough search of the literature and concluded that there were only three other reports of cases that could be considered similar to Vogt's case of spear cataract. These were the cases of Gifford,[4] Cords,[5] and Gifford and Puntenney.[6]

Gifford,[4] in 1924, reported a case resembling that of Vogt. This was an 8-year-old boy with cataracts "in which similar crystals were arranged more regularly in the axial area so as to resemble two fir trees with their bases together in the center of the lens, the tips coming nearly to the anterior and the posterior capsule." This child also had congenital ptosis and nystagmus.

In 1926 Cords [5] described two sisters, aged 21 and 24, each with a unilateral cataract with crystalline needles. This cataract was described as a whitish central opacity, resembling a snowball, out of which projected needle-like crystals. There was a familial history of cataract.

In 1937 Gifford and Puntenney [6] reported the case of a 20-year-old girl who had always had defective vision. A discission had been done on the right eye at the age of 13. The

Fig. 1.—Clinical appearance of cataract composed of crystals, as seen with the biomicroscope; right eye.



Received for publication Oct. 19, 1955.

From the Department of Ophthalmology, U. S. Naval Hospital.

The opinions or assertions contained herein are the private ones of the writer's and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

* Romer, A., cited by Vogt.[2]

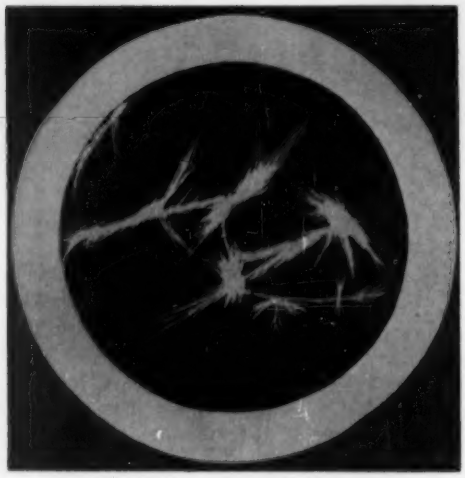


Fig. 2.—Clinical appearance of cataract composed of crystals, as seen with the biomicroscope; left eye.

left eye showed a cataract in which the opacity consisted of crystals in aggregates of needles. The center of the lens contained a circular mass just behind the anterior Y-suture. Additional collections of crystals formed a concentric crown around the central mass, with a few scattered crystals in the zone between the two. There was a thin layer of normal cortex external to the outer layer of crystals. This lens was extracted, and chemical analysis indicated that the crystals were calcium sulfate. In this case, too, there was a familial history of cataracts.

REPORT OF A CASE

A 22-year-old white man was seen on March 23, 1955, desiring refraction. He gave no history of previous eye difficulty, trauma, or inflammation. He did not complain of inability to see or of any change in his visual status. Examination revealed bilateral lens opacities. The right lens contained many yellowish-white needle-like crystals, some of which were iridescent, extending in random directions, singly and in groups throughout the lens, with complete disregard of anatomic structure. There were a few scattered areas of denser opacity which resembled a coagulated group of crystals. The major portion of the opacities was in the central portion of the lens (Fig. 1). The left eye showed a similar picture but to a slightly less degree (Fig. 2). The remainder of the eye examination was within normal limits. Visual acuity was 20/30 O. D., corrected to 20/25 with +0.50 sph⌒—0.50 cyl, ax 180, and 20/60 O. S., corrected to 20/25 with +1.00 sph⌒—2.25 cyl, ax 10. There was no apparent familial history of cataract. However, the family was not available for examination.

SUMMARY

There are in the literature four reports of a rare congenital cataract characterized by the appearance of needle-like crystals, situated in the axial or central portion of the lens, which appear in a random fashion, with no apparent relation to the anatomic structure of the lens. This was first described by Vogt in 1921 and given the name "spear cataract." Previous authors have concluded that this condition is transmitted in a dominant manner. An additional case is presented.

The drawings were made by Miss Julia Loyd, of the Department of Ophthalmology, Hospital of the University of Pennsylvania, and the Medical School of the University of Pennsylvania.

U. S. Naval Hospital, Philadelphia.

REFERENCES

1. Vogt, A.: Weitere Ergebnisse der Spaltlampenmikroskopie des vorderen Bulbusabschnittes: III. Angeborene und früh erworbene Linsenveränderungen, von Graefes Arch. Ophth. **107**:196, 1922, p. 237.

2. Vogt, A.: Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges, Berlin, Springer-Verlag, 1931, Vol. 2, p. 448.

3. Renard, G., and Laporte, P.: Les Cataractes congénitales à cristaux, Arch. opht. **11**:739, 1951.

4. Gifford, S. R.: Congenital Anomalies of the Lens as Seen with the Slit Lamp, Am. J. Ophth. **7**:678, 1924.

5. Cords, R.: Kayser-Fleischerscher Ring bei Pseudosklerose, Klin. Monatsbl. Augenh. **76**:125, 1926.

6. Gifford, S. R., and Puntenney, I.: Coralliform Cataract and New Form of Congenital Cataract with Crystals in Lens, Arch. Ophth. **17**:885, 1937.

Diathermic Surgery for a Case of Angiomatosis Retinae

BERNARD KRONENBERG, M.D., New York

Angiomatosis retinae is one of a group of congenital, hereditary, and familial diseases known as phacomatoses (φακός, meaning birthmark). Angiomatosis of the retina has been known to ophthalmologists for a long time and has been reported in one form or another since 1879 (Panas and Rémy [1]). Von Hippel [2] established it as an ocular clinical entity in 1904. It was not until 1926 that Lindau [3] recognized its relationship to cerebellar cysts. Since then it has been frequently designated as von Hippel-Lindau disease, but such designation is valid only if a cerebellar cyst can be demonstrated.

Angiomatosis retinae is a rare disease. About 150 cases have been reported in the literature. The lesion occurs in 36% of the cases bilaterally. In the unilateral cases the left eye is more frequently involved than the right. Males are more frequently affected. The disease has a definite hereditary trend.

The disease is not stationary. The rate of progress from the initial vascular dilatations to the final stage of glaucoma, however, is very variable. Cases have been observed without any change over a period of many years and then the disease suddenly begins to progress, for reasons unknown to us.

The characteristic dilatation of the vessels in the early stage is such that it is sometimes difficult to differentiate a retinal artery from a retinal vein. Both usually feed into an angiomatous formation in the periphery. This formation may be red or yellow-gray in color and circular, oval, or irregular in shape. After a while the retinal vessels become very dilated and tortuous; they may even have sausage-shaped swellings. Small subretinal yellowish spots appear, which may be exudates. A macular star may also appear. The yellowish patches can coalesce to form large subretinal sheets. In some sections partial retinal detachment can occur. The detachment then progresses until the whole retina is detached. Secondary glaucoma sets in, and the vision is permanently destroyed.

The prognosis is essentially poor. Some cases, however, remain latent indefinitely. Patients who are seen in the early stages should have some form of therapy to prevent the progression of the disease. The later stages show retinal detachments, extensive exudates, and hemorrhages. At that point no therapy is of any use.

The therapy of angiomatosis retinae must seek to destroy the growth. It is most successful in early cases. Various methods have been used in an attempt to destroy the lesion. Radium applications were employed by Holm,[4] Traquair,[5] Moore,[6] and others. Cordes and Hogan [7] reported on the successful use of x-ray therapy. Recently Cordes and Schwartz [8] reported on an 11-year follow-up of a case treated with x-rays and previously reported by Cordes and Hogan. The patient had retained 20/20 vision in the treated eye. Weve [9] used surface coagulation with diathermy, as well as diathermy punctures. Since Weve reported the successful use of diathermy, other reports, by Kaye,[10] Lewis,[11] and others using diathermy, have appeared in the literature.

The cystic lesion in angiomatosis, being in the periphery, lends itself easily to treatment by diathermy. In localizing the growth during the operation the same technique can be used as that employed in localizing a tear

Received for publication Oct. 31, 1955.

in the retina when operating for detachment. The patient presented here was treated by diathermy coagulation and punctures.

REPORT OF CASE

I have had the opportunity to observe this patient at regular intervals over a period of six years, before surgery. I have also observed this patient for two and a half years postoperatively.

A white woman, age 36, first consulted me in September, 1946, for a routine examination. The patient had a moderate degree of myopia and myopic astigmatism in both eyes and with correction had 20/20 vision in each eye. A fundus examination revealed a normal retina in the right eye. The left eye, however, showed a marked dilatation of the vessels from the optic nerve to the periphery of the retina around 12 o'clock. There the vessels appeared to join with a grayish-white mass of irregular shape. The mass was about 2 disc diameters in size. Halfway between the optic nerve and the mass some yellowish exudates were visible. A diagnosis of angiomatosis retinae was made and contact made with her medical physician. No evidence was found of any cerebellar involvement. The visual fields showed no defect. The patient was observed at regular intervals until September, 1947, when she first complained of any symptom, i. e., flashes of light. The fundus picture was still the same, however. The patient was seen at six-month intervals thereafter, and no change was found in vision, fields, or the fundus picture. It was not until February, 1951, that there was any significant change in the symptoms. She then complained of a veil and an increase in the flashes of light. The fundus showed a dehiscence of the anterior layer of the retina above and temporally. It looked like a flat detachment. There was a loss in the visual field below and nasally. The patient was observed at monthly intervals, and by October, 1951, the detachment had become slightly more marked. Vision through the entire period was 20/20 in the left eye. At this point I suggested surgery to the patient. She consulted another ophthalmologist and then refused operation on the basis of his advice. I continued to observe her at monthly intervals until July 15, 1952. At this time the picture was essentially the same as in February, 1951. The vision was 20/20; the visual field defect was unchanged, and the fundus picture was the same. She returned two weeks later, stating that she had suddenly lost vision in the left eye. The vision with correction was then 20/50. In the macula there was a star-shaped formation. The detached area of the retina was more prominent. In the course of a few days the vision dropped to 2/400 and the macula became edematous. The patient was given cortisone acetate 100 mg. daily until the edema receded and the vision returned to 20/200. On Sept. 8, 1952, a diathermy operation was performed.

On the first thorough postoperative examination, one month later, the vessels were found to be shrunken. The cyst was collapsed and flat. The detached area contained a small hemorrhage but was flat. In the course of the next months the hemorrhage disappeared and the vision returned to 20/40. The patient complained of flashes of light in both eyes through this entire period.

It is now two and a half years since the operation. The vision has remained stationary at 20/40+. The cyst is flat, the vessels about normal. The detached area is replaced by extensive chorioretinitis. The field defect is the same. The macula is clear of any exudate. The fundus shows no exudates.

Operative Technique.—The sclera over the cyst and the retinal detachment was exposed in the usual fashion. A single Walker pin was then placed in the area of the cyst and observed with an ophthalmoscope. It was found to be close to the cyst, and a few more pins were then placed around the cyst. Some pins were placed on either side of the dilated vessels going toward the optic nerve. Surface ball-electrode applications were applied, in addition to the pins. This was done in an attempt to sclerose the vessels. Attention was then given to the detached area. A series of ball-electrode applications were applied to the sclera, and, finally, seven Walker pins were placed in the area to permit the fluid to drain off. The procedure was constantly observed with the ophthalmoloscope. No hemorrhage occurred. The patient was then treated postoperatively as in any other detachment.

CONCLUSION

The patient was presented to demonstrate the surgical treatment of angiomatosis retinae and to emphasize the advisability of early surgery. The sequence of the changes in the fundus picture was of great clinical interest. Evaluation of these changes must lead to the realization that surgical therapy should be instituted as early as possible. Nothing is gained by waiting. The disease is progressive, and earlier therapy may therefore prevent the loss of vision. The patient presented here might have had better vision in the eye operated on if surgery had been carried out at the first sign of activity. Having waited until she had macular edema, we certainly could not expect as good a result as though

we had operated earlier. This case is certainly an argument for early surgery.

On the other hand, the deterrent factor to early surgery is the fear of intraocular hemorrhages. Sometimes hemorrhage cannot be avoided. At other times it may result from improper diathermy punctures. However, hemorrhage as a complication is not always disastrous. For example, this patient had a small hemorrhage that must have occurred in the postoperative period, since it was not observed at the operation. Despite that, the retina reattached and the patient has had no difficulty since the operation.

737 Park Ave. (21).

REFERENCES

1. Panas, F., and Rémy, A.: Anatomie pathologique de l'oeil, Paris, A. Delahaye & Cie, 1879.

2. von Hippel, E.: von Graefes Arch. Ophth. **59**:83, 1904.

3. Lindau, A.: Acta path. et microbiol. scandinav., Supp. 1, 1926.

4. Holm, E.: Klin. Monatsbl. Augenh. **59**:319, 1917.

5. Traquair, H. M.: Tr. Ophth. Soc. U. Kingdom **53**:311, 1932.

6. Moore, R. F.: Proc. Roy. Soc. Med. **26**:1036, 1933.

7. Cordes, F. C., and Hogan, M. F.: Arch. Ophth. **23**:253, 1940.

8. Cordes, F. C., and Schwartz, A.: Tr. Am. Ophth. Soc. (1952) **50**:227, 1953.

9. Weve, H. J. M.: Tr. Ophth. Soc. U. Kingdom **59**:43, 1939.

10. Kaye, H.: Arch. Ophth. **25**:443, 1941.

11. Lewis, P. M.: Arch. Ophth. **30**:250, 1943.

The Spherophakia-Brachymorphia Syndrome

J. WILLIAM ROSENTHAL, M.D.
and
H. WARNER KLOEPFER, Ph.D., New Orleans

In 1939 Marchesani[1] described a syndrome consisting of brachydactyly, spherophakia, and glaucoma in four patients. Since then 27 additional patients have been described by various authors. Since no instances of this syndrome have been recorded in the United States, the following study of five patients showing the complete syndrome is reported, with a summary of the genetic findings in the two involved families.

The spherophakia-brachymorphia syndrome, sometimes referred to as Marchesani's syndrome, is characterized by short stature (Fig. 1); short, stubby fingers (Fig. 2), and mental retardation, in conjunction with spherophakia, microphakia, ectopia lentis, index myopia, and glaucoma. In addition, in this study a large *atd* angle (Fig. 3) was found in the fully developed cases, as well as in heterozygous carriers. The syndrome is hereditary, showing essentially a recessive tendency.

REPORT OF CASES

The following patients with the fully developed syndrome were observed in two families. The numbers used to identify them are the same as those used in a report of the genetic study by Kloepfer and Rosenthal.[2a]

The first figure indicates the family, and the remaining figures indicate the position of the patient in the family tree.

Received for publication July 18, 1955.

From the Departments of Ophthalmology and Anatomy of Tulane University of Louisiana School of Medicine.

This study was supported in part by a grant from the National Council to Combat Blindness, Inc.

CASE 1-96.—A 47-year-old white man of French descent presented himself for treatment because of pain in the right eye, which had been recurrent for several years. The left eye had been enucleated at the age of 21 because of trauma.

Examination of the right eye revealed that the lens was dislocated in the vitreous. On the second day in the hospital the lens was in the pupil, and on the third day it was in the anterior chamber. The lens was extracted intracapsularly and a complete iridectomy made, without vitreous loss. The patient's syndrome diagnosis was not known at that time, and therefore the lens was not studied. Six weeks later the visual acuity was corrected to 20/20 with +10.00 sph ⌣ +2.00 cyl, ax 110. The intraocular pressure was 25 mm. Hg (Schiøtz). Visual field studies showed a 5-degree circle (12.5/330 white) without glasses.

General physical examination revealed the stature to be short (151.1 cm., with a span index of 89.0). The fingers were short and stubby, with a finger-

Fig. 1.—Siblings of Kindred 1, showing spherophakia-brachymorphia syndrome. From left to right they are as follows: 1-96, affected propositus; 1-102, affected sister; 1-99, normal brother (5 ft. 8 in. tall); 1-105, affected brother.

Fig. 2.—Brachydactyly in a member (Pedigree 1-94) with spherophakia-brachymorphia syndrome.

palm index of 57.24. The *atd* angles were large, the sum of the largest *atd* angles in the right and left hands being 127 degrees.

Case 1-105.—A 33-year-old white man, brother of Case 1-96, complained of seeing rainbows and of intermittent episodes of acute pain in the right eye. He had worn glasses since the age of 9 years and had had the left eye removed, apparently in an attack of acute glaucoma, when 24 years of age.

Examination revealed a prosthesis in the left socket. The visual acuity of the right eye was counting fingers at 6 ft. (1.8 meters) but was corrected with —8.00 sphere to 20/30. Externally the eye appeared normal, but slit-lamp and biomicroscopic examination revealed that the anterior chamber was slightly shallow because the spherophakic lens was pushing the iris forward centrally. The intraocular pressure was 55 mm. Hg, and ophthalmoscopic examination disclosed a glaucomatous cup.

General physical examination revealed a short stature (153.0 cm.), short fingers (finger-palm index 63.85), span index 96.1, sum of *atd* angles 128 degrees.

The intraocular pressure dropped to 50 mm. Hg (Schiøtz) after 1 drop of 2% pilocarpine hydrochloride, which instillation was continued four times a day thereafter. However, on the following morning the patient developed an acute attack of glaucoma with a pressure of 65 mm. Hg. This was relieved in 15 minutes by 1 drop of 10% aqueous solution of phenylephrine hydrochloride. Several days later a peripheral iridectomy was made through an ab externo incision. Since then the intraocular pressure has remained normal, and there has been no further complaint of seeing rainbows.

Case 1-102.—A 41-year-old white woman, sister of Patient 1-96, complained of poor vision. The right eye had been removed in 1935, during an attack of acute redness and pain. Approximately one year later she had an operation, of unknown type, on the left eye, and in 1942 she had a cataract removed from the left eye.

Examination, which was made on a field trip as a part of the family study, revealed a prosthesis in the right socket. The visual acuity of the left eye was finger counting at 15 ft. with and without correction. Rotations of the globe were normal. There were two small filtering blebs at the upper limbus, one at 12 o'clock and one at 1 o'clock. The eye was aphakic, with a hammock pupil, and ophthalmoscopic examination revealed a pale nerve head with a deep glaucomatous cup, but the eye was soft to palpation.

General physical examination disclosed the typical body conformation of the syndrome; height, 137.4 cm.; finger-palm index, 54.67; span index, 91.7, and sum of *atd* angles, 158.5 degrees.

Case 1-94.—A 49-year-old white woman, sister of Case 1-96, was examined on a field trip in August, 1953. Poor vision, of 25 years' duration, had been treated by drops and an operation on each eye.

Examination revealed the visual acuity was reduced to light perception in each eye. There was

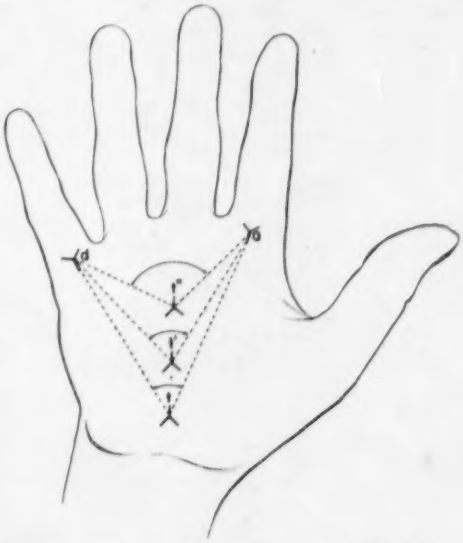


Fig. 3.—The *atd* angle is described by the intersection of dotted lines extended from the *a* and *d* digital triradii to the highest axial triradius on the palm, which may be located in the *t*, *t'*, or *t''* position. A triradius is formed by epidermal ridges running in three directions past a common point.

a filtering bleb in each eye, apparently the result of a trephine operation, and the eyes were soft to palpation. A small cataractous lens was observed in front of the pupil in the anterior chamber of the right eye. The deeper structures of the eye were not visible through the slit-like pupillary space above the lens. The pupil of the left eye was drawn upward, almost into the old corneoscleral scar. The iris showed iridodonesis. The lens and deeper structures of the eye were not seen.

General examination revealed short stature (140.7 cm.), with a span index of 92.39; short, stubby fingers (finger-palm index 58.40), and large *atd* angles (145.5 degrees).

In October, 1953, the patient was admitted to the hospital because of a perforated corneal ulcer of the right eye of approximately 12 days' duration. The eye was enucleated, and microscopic examination revealed a perforated, partially necrotic cornea and endophthalmitis, with extensive destruction of the intraocular structures.

Following the enucleation, x-ray studies of the bones of the right arm and leg and both feet and hands showed "normal calcification, symmetry, and shape, but the bones were smaller than normal." The sella turcica was of normal size.

CASE 2-19.—A 40-year-old white man of Italian descent complained of intermittent attacks of pain in the right eye and headaches of several months' duration. He had worn glasses since childhood and thought his vision was good.

Examination in the winter of 1952 revealed the visual acuity to be 20/60 in the right eye and 20/80 in the left eye with his glasses. The anterior chambers were deep, and each eye showed iridodonesis, spherophakia, and glaucomatous cupping of the nerve head. The intraocular pressure was 55 mm. Hg (Schiøtz) in the right eye and 35 mm. Hg in the left eye. Although miotic drops were prescribed, the patient did not use them regularly. During the following weeks the intraocular pressure of the right eye varied from 21 and 65 mm. Hg and that of the left eye between 18 and 35 mm. Hg. Although he was advised to have iridectomies, he refused and subsequently suffered two attacks of acute congestive glaucoma in the right eye. These were successfully controlled by intensive miotic therapy, combined with retrobulbar injection of procaine, sedation, and dehydration. He has consistently refused surgical treatment. After recovery from the second attack of acute glaucoma the visual field of the right eye showed some enlargement of the blind spot, but the periphery extended approximately 50 degrees from fixation in all meridians (3/330 white). The field of the left eye was similar to that of the right eye, but slightly larger in peripheral extent. Visual acuity of the right eye was 20/70 with —11.00 sph⁀—0.75 cyl, ax 90, and that of the left eye was 20/25 with —4.00 sph⁀—0.50 cyl, ax 45.

General physical examination revealed a short stature (155.0 cm., with a span index of 97.7); short, stubby fingers (finger-palm index 69.47), and large *atd* angles (119 degrees).

EYE FINDINGS

Spherophakia, as the name indicates, is characterized by an increased curvature of the anterior and posterior surfaces of the lens. It is recognized easily by slit-lamp microscopy and is found in all cases of the complete syndrome.

In addition to being spherical, the lenses in all cases of the complete syndrome are smaller and weigh less than normal.[2] At times this microphakia may be masked by the spherophakia. Because of both the spherophakia and the microphakia, the zonular fibers are exposed to direct view upon dilatation of the pupil. Iridodonesis is observed because of the lack of support of the iris by the small sperical lens or because of subluxation of the lens. Ectopia lentis is common, and, although much emphasis has been placed on the direction of the displacement, each case presents its own problem in this manifestation. It probably develops as a result of relatively minor trauma to the weakened zonule. The lens may be dislocated into the vitreous or anterior chamber, and at times may pass from one location to the other. In some cases the lens may be caught in the pupil.

Stadlin and Klein [2] state:

> The syndrome of Marfan, as well as that of Marchesani, should be classified among the congenital systematized affections of the mesenchymal tissue. Contrary to the syndrome of Marfan, which should be considered, according to Weve, as a hypoplastic form of congenital mesodermic dystrophy, we have in the type of Marchesani the hyperplastic variant of the anomaly of the mesodermal tissue.
>
> The fact that we found it affects the crystalline lens, an ectodermal organ, in these two syndromes is not in opposition to the theory of the mesodermal origin of these two disorders. In fact, we know that the former is secondary to a dysplasia of the ciliary body, which is underdeveloped, and, on account of that, causes ectopia of the crystalline lens. One notes near the deficiency of the ciliary body an

abnormal length and a partial rent of the zonular fibers, such as Vogt had described. This congenital defect explains, according to him, the spherophakia, as well as the microphakia. The traction of the zonular fibers in the crystalline lens necessary for its normal development being markedly diminished on account of this zonular deficiency, the lens remains in its primitive state, possibly in a spherical form, and increases only a little in later development.

Myopia in this syndrome probably is due entirely to the spherophakia. It is index myopia. The amount is contingent on the lens curvature and thus differs from case to case. When the lens is extracted, a correcting lens of the usual strength is required for the aphakia. One of our propositi required a lens of +10.00 sph⊃+2.00 cyl, ax 180 for a visual acuity of 20/20 in his only eye after removal of the lens. This is not in agreement with Stadlin and Klein, who term the myopia as axial, since one of their patients was corrected by +1.00 sph⊃+3.00 cyl, ax 90 after discission of the lens. However, another of their patients required +7.00 sph⊃+2.00 cyl, ax 130 after discission. Probably the occurrence of axial myopia should be expected, in addition to index myopia, as a coincidental finding in a certain percentage of these cases.

Glaucoma is of the pupillary-block type. It occurs, to quote Probert,[8] (*a*) without a dislocated lens, and is due to the soft anterior lens substance blocking the pupillary zone and hindering the flow of aqueous from the posterior to the anterior chamber. It also occurs (*b*) as a complication of dislocation (1) by irritation of the ciliary body, (2) by blocking of the angle, or (3) by complete luxation into the anterior chamber." The dislocated lens also may become lodged in the pupillary sphincter. As would be expected, repeated minor attacks of acute congestive episodes occur, which may eventually lead to chronic narrow-angle glaucoma, with restricted fields and glaucomatous cupping of the nerve head. In six eyes of this series, these attacks resulted in actual or functional loss of the eye. One attack, it is believed, was brought on by application of pilocarpine, which at first lowered intraocular pressure but later caused an acute elevation.

Several findings reported in the literature have not been confirmed in cases of the present series. They are persistent pupillary membrane, iridodonesis in children (with myopia and ectopia lentis), ptosis, nystagmus, flat anterior chamber, and paresis of gaze. Several cases in our series had only one eye, and therefore coordination could not be determined. There were no apparent muscle pareses.

Ptosis was not observed in these cases. The palpebral fissure of one of the propositi was narrow, but the narrowing was due to orbicularis spasm. No case was obliged to hold the head back in order to see. We do not believe that the syndrome encompasses extraocular muscle paresis in any form.

As was recorded by Stadlin and Klein,[2] these patients, in many ways, were infantile and mentally retarded. They were of a low social status, had had little formal education, showed ability and incentive to work in only two cases, and exhibited a bad memory and defective faculties of comprehension. Marchesani,[1] on the other hand, reported some of his patients to be intelligent.

GENETICS

In one family, of French descent (Fig. 4), 4 out of 12 siblings have the full syndrome. In another family, of Italian descent (Fig. 5), one of seven siblings is affected. Although 91 relatives of these affected members were examined and inquiries made about 777 additional relatives, no other cases of the full syndrome were found. The parents in one family are related. An autosomal recessive mode of inheritance for the full syndrome is apparent, and this genetic explanation is compatible with all the previous studies listed in Table 1 except in Families 9 and 12.

If the gene in Families 9 and 12 is a different entity and is located at a different chromosomal locus from the one causing the syndrome in all other families, a consanguinity rate of 50% (a value suggesting a

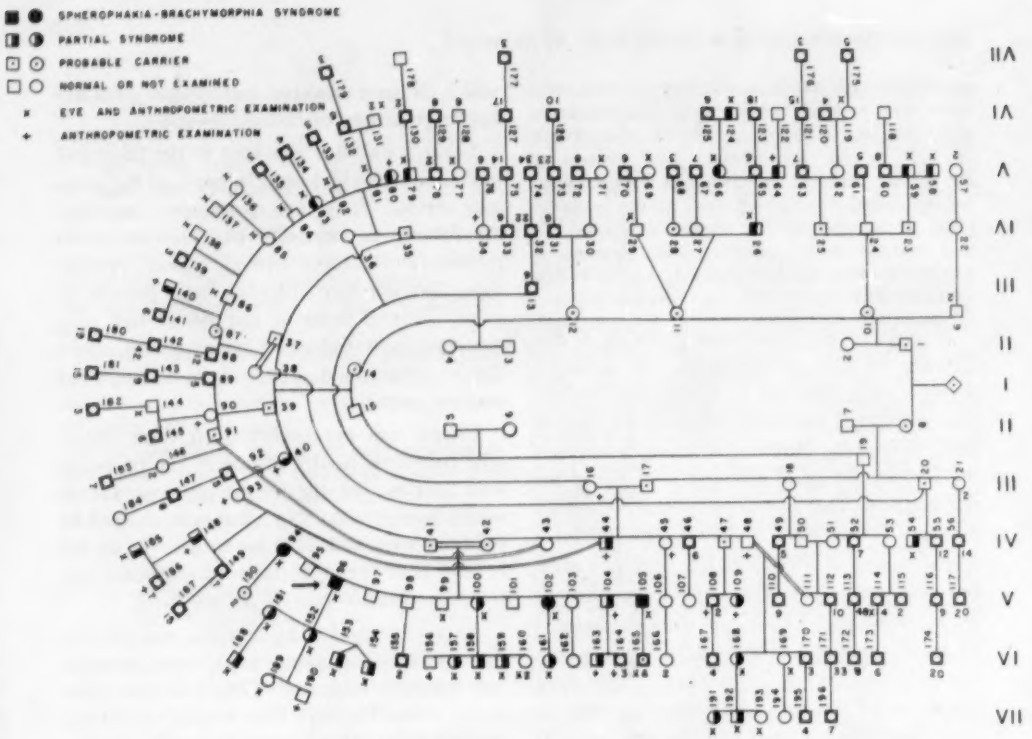


Fig. 4.—Pedigree of Kindred 1, showing recessive types of the spherophakia-brachymorphia syndrome in a family of French descent. Reference numbers of members are above the symbols; numbers below the symbols are the numbers of members, if more than one, represented by a single symbol.

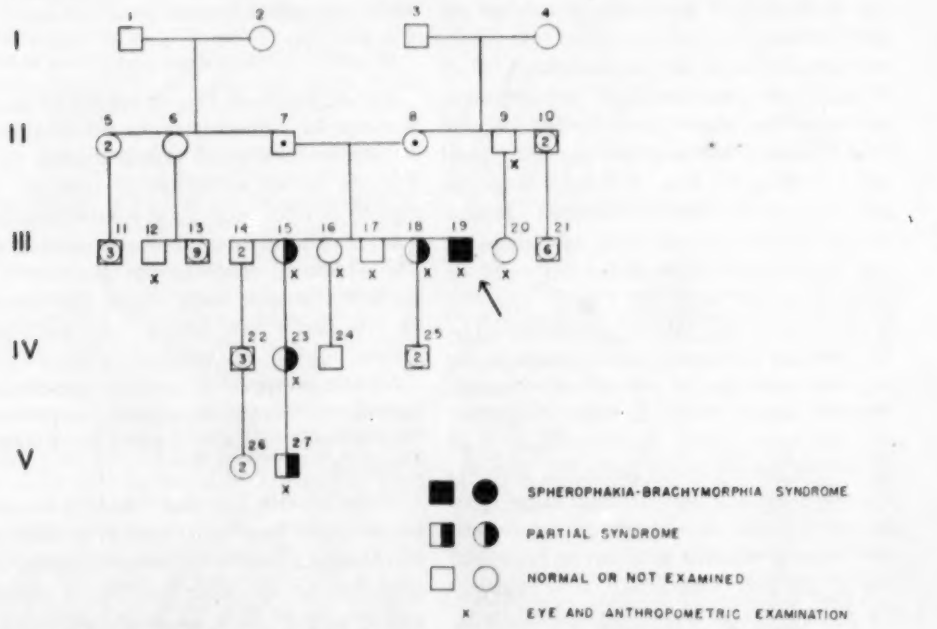


Fig. 5.—Pedigree of Kindred 2, showing recessive type of spherophakia-brachymorphia syndrome in a family of Italian descent. Reference numbers of members are above the symbols; numbers within symbols are the numbers of members, if more than one, represented by a single symbol.

very rare recessive gene) is obtained when the two families herein reported are combined with the 10 previously reported, in which the syndrome was said to be caused by a recessive gene. Probert [8] is uncertain about the mode of inheritance, and his family is not included with those of the recessive type. Since recessive genes may cause eye and anthropometric deviations in the direction of the syndrome in heterozygotes (persons who possess one gene for the syndrome, in contrast to homozygotes, who possess two genes for the syndrome), a less plausible, but possible, explanation for the dominant type of inheritance in Families 9 and 12 is that environmental differences caused by other genes or by nongenetic factors have made it possible for the usually recessive gene to produce the full syndrome in these two situations.

The combined male-female sex ratio in families of the recessive type is 11:11, in contrast to a 5:9 ratio for families of the dominant type. However, the 1:2 sex ratio suggested by these two families of the dominant type is not based on sufficient numbers to be statistically significant. If genes causing the dominant and recessive types are at different chromosomal loci, an effort should be made in future studies to discover minute clinical and subclinical differences which might be useful in distinguishing the two types.

Although a fair sampling of ages from 3 months to adulthood was obtained in 22 children in these families, no child was found to have the full syndrome (double-gene effect). There were no young siblings of the cases reported above, and, although there were four other consanguineous marriages in one kindred, there was no evidence that the parents of these matings were both heterozygotes. Therefore, no double-gene effect was found in their children.

Other authors have theorized upon the basic tissue involved in the pathological process of the spherophakia-brachymorphia syndrome and have come to the conclusion that this is a mesodermal dysplasia. However, the lens is not mesodermal, but is ectodermal, and is primarily involved in the syndrome. In order to explain this apparent contradiction, we have considered the syndrome to be a gene defect that expresses itself in both mesodermal and ectodermal derivatives.

TABLE 1.—*Summary of Studies of Spherophakia-Brachymorphia Syndrome*

Family	Author	Date	Consanguinity Reported	No. of Affected			Probable Mode of Inheritance
				Males	Females	Total	
1	Weill [4]	1902	None	0	1	1	Recessive
2	Marchesani [1]	1939	None	1	0	1	Recessive
3	Marchesani [1]	1939	None	2	1	3	Recessive
4	Meyer and Holstein [14]	1941	First cousin	1	3	4	Recessive
5	Schmid [3]	1946	None	1	0	1	Recessive
6	Diethelm [10]	1947	First cousin	1	1	2	Recessive
7	Stadlin and Klein [9]	1948	Second cousin	0	1	1	Recessive
8	Seelemann [5]	1949	None	1	0	1	Recessive
9	Rousseau and Hermann [7]	1949	None	3	6	9	Dominant
10	Arjona [12]	1962	Cousins	1	1	2	Recessive
11	Arjona [13]	1962	Second cousin	0	1	1	Recessive
12	Probert [8]	1963	None	2	3	5	?
13	Rosenthal and Kloepfer [23]	1965	None	1	0	1	Recessive
14	Rosenthal and Kloepfer [23]	1965	First cousin	2	2	4	Recessive

ANTHROPOMETRIC FINDINGS

Kloepfer and Rosenthal [23] report eye and anthropometric observations in the nonaffected relatives of the five cases presented here that may be useful in distinguishing the heterozygotes from the homozygous-normal and the homozygous-affected. In their study, short stature, short fingers, and a wide *atd* angle of the palm were found to

be the most useful stigmata for supplementing eye findings in diagnosis and for counseling within families.

GENETIC COUNSELING

Since the disease has been reported as dominant in 2 families and as recessive in 10, it is necessary to determine the type of inheritance by study of the family before advice on recurrence can be given. In dominant types half the siblings and half the offspring of affected persons will be expected to carry the gene, but too little information is available to predict that all of these gene carriers will show the full syndrome.

In the recessive type, one-fourth of the subsequent siblings of the first affected member will be expected to show the full syndrome, and one-half will be expected to be carriers. All the offspring of affected persons who marry homozygous normals will be heterozygous (single-gene) carriers. Although 92% of these carriers will be expected to show short stature, 71% short fingers, 45% wide *atd* angles, and 40% ocular manifestations of the partial syndrome, none will be expected to develop the full syndrome. The offspring of affected persons who marry heterozygous carriers for the same gene would be expected to be 50% affected and 50% carriers. The offspring of two fully affected persons would be expected to be fully affected in all cases. Matings of the two latter types, however, are expected to be extremely rare. These theoretical expectations are based on the assumption that all recessive genes of the syndrome occupy the same chromosomal locus.

DIFFERENTIAL DIAGNOSIS

A comparison of findings in Marfan's syndrome and in the spherophakia-brachymorphia syndrome is made in Table 2.

Weill [4] reports one case of arachnodactyly with nanism that probably was actually an unrecognized case of the spherophakia-brachymorphia syndrome. His second case of nanism cannot be classified because of the description of large hands.

OCULAR THERAPY

Treatment is largely directed toward the prevention or relief of glaucoma that results primarily from pupillary block. However, repeated acute episodes of pupillary-block glaucoma may result in peripheral anterior synechia and chronic glaucoma, and occasionally secondary glaucoma may reuslt from prolonged dislocation of the lens in the vitreous.

Appropriate studies of anatomical relationships, lens position, visual acuity, visual field, and intraocular pressure will guide in determining the choice of medical or surgical therapy.

Early acute glaucomatous attacks should be treated with the aim of relieving pupillary block, usually by dilation of the pupil. If the lens is producing pupillary block intermittently with miosis, a peripheral iridectomy should be made, and, in general, the lens should be removed when (1) it is almost or

TABLE 2.—*Comparison of Arachnodactyly and Spherophakia-Brachymorphia Syndrome* *

Arachnodactyly	Spherophakia-Brachymorphia
1. Dolichocephaly	1. Brachycephaly
2. Long asthenic build; tapering fingers; little subcutaneous fat; poorly developed musculature; kyphosis and congenital abnormalities of heart	2. Short, pyknic built; short fingers and toes; good subcutaneous fat; well-developed musculature
3. Pointed sternum	3. Broad thorax
4. Overextensibility of joints	4. Reduced joint mobility
5. No glaucoma	5. Glaucoma
6. Ectopia lentis sometimes congenital	6. Ectopia lentis occurring later in life
7. Lens of normal size	7. Microphakia
8. Lens of normal shape	8. Spherophakia
9. Dominant inheritance	9. Recessive inheritance, usually

* Modified from Seeleman [5] and Probert.[3]

entirely subluxated in the vitreous or anterior chamber, (2) it is in place but causing uncontrolled pupillary-block glaucoma, or (3) it is straddling the pupillary aperture. Such early treatment may prevent the development of chronic glaucoma. However, later cases may require filtering procedures in addition to extraction of the lens.

Vision, of course, should be improved to the maximum by the use of lenses. Of necessity, these will be either strongly myopic or strongly hyperopic, depending upon the presence or absence of the crystalline lens.

SUMMARY

Five new cases of the spherophakia-brachymorphia syndrome are described. Four cases occurred in one family. In addition to the usual findings of spherophakia, microphakia, index myopia, ectopia lentis, secondary glaucoma, brachydactyly, short stature, and small span index, study of the two families revealed larger *atd* angles in patients with the full syndrome. In these two families the disease was manifested as an autosomal recessive, with partial development of the syndrome in heterozygous carriers.

Glaucoma usually develops as a result of pupillary block, or may result from dislocation of the lens. Early treatment by iridectomy or iridectomy and extraction of the lens may prevent serious visual loss.

Dr. James H. Allen, Chairman of the Department of Ophthalmology, and Dr. Harold Cummins, Chairman of the Department of Anatomy, gave help during the course of this study and read and criticized the manuscript.

REFERENCES

1. Marchesani, O.: Brachydactyly and Congenital Spherical Lens, Klin. Monatsbl. Augenh. **103**: 392-406 (Oct.-Nov.) 1939.

2. Stadlin, W., and Klein, O.: Congenital Ectopia of the Crystalline Lens with Spherophakia and Brachymorphia, Accompanied by Paresis of Gaze (Syndrome of Marchesani), Ann. ocul. **181**: 692-701 (Nov.) 1948.

3. Probert, L. A.: Spherophakia with Brachydactyly, Am. J. Ophth. **36**:1571-1574 (Nov.) 1953.

4. Weill, G.: Ectopia of the Crystalline Lens and General Malformations, Ann. ocul. **169**:21-44 (Jan.) 1932.

5. Seelemann, K.: Brachydactyly and Congenital Spherical Lens, Ztschr. Kinderh. **67**:1-6, 1949.

6. Shapira, T. M.: Micro- and Spherophakia with Glaucoma, Am. J. Ophth. **17**:726-735 (Aug.) 1934.

7. Rousseau and Hermann: Congenital Ectopia of the Crystalline Lens with Brachymorphic Condition (Dwarfism), Bull. et mém. Soc. franc. opht. **62**:369-373, 1949.

8. Schmid, A. E.: Light Reflexes in Spherophakia, Ophthalmologica **111**:359-364 (June) 1946.

9. Lisch, K.: Microphakia-Spherophakia and Ectopia of the Lens, von Graefes Arch. Ophth. **144**:628-642 (July) 1942.

10. Diethelm, W.: Ectopia of the Lens Without Arachnodactyly and Its Relations to Ectopia of the Lens and Pupil, Ophthalmologica **114**:16-32 (July) 1947.

11. Arjona, J., in discussion on Benito, H.: Marfan's Syndrome, Madrid Ophthalmological Society, March 13, 1953, Proceedings, Am. J. Ophth. **37**:791 (May) 1954.

12. Arcoja, J.: Syndrome of Marchesani, Arch. Soc. oftal. hispano-am. **12**:1167 (Oct.) 1952; abstracted, Am. J. Ophth. **36**:1018-1019 (July) 1953.

13. Brailsford, J. F.: Familial Brachydactyly, Brit. J. Radiol. **18**:167-172 (June) 1945.

14. Meyer, S. J., and Holstein, R.: Spherophakia with Glaucoma and Brachydactyly, Am. J. Ophth. **24**:247-257 (March) 1941.

15. Barber, A. N.: Embryology of the Human Eye, St. Louis, C. V. Mosby Company, 1955, p. 154.

16. Mann, I.: Developmental Abnormalities of the Eye, London, The Cambridge Press, 1937, p. 154.

17. Kirby, D. B.: Surgery of Cataract, Philadelphia, J. B. Lippincott Company, 1950, p. 177.

18. Walsh, F. B.: Clinical Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947, p. 457.

19. Cummins, H., and Midlo, C.: Finger Prints, Palms and Soles, Philadelphia, The Blakiston Company, 1943, p. 309.

20. Watson, E. H., and Lowrey, G. H.: Growth and Development of Children, Chicago, The Year Book Publishers, Inc., 1952.

21. Penrose, L. S.: The Distal Triradius on the Hands of Parents and Sibs of Mongol Imbeciles, Ann. Human Genet. **19**:10, 1954.

22. McKusick, V. A.: The Cardiovascular Aspects of Marfan's Syndrome: A Heritable Disorder of Connective Tissue, Circulation **11**:321 (March) 1955.

23. Kloepfer, H. W., and Rosenthal, J. W.: Possible Genetic Carriers in the Spherophakia-Brachymorphia Syndrome, Am. J. Human Genet., to be published.

Ocular Manifestations of Systemic Cystinosis

DAVID G. COGAN, M.D.
TOICHIRO KUWABARA, M.D.
JIN KINOSHITA, Ph.D.
DAVID SUDARSKY, M.D.
and
HENRY RING, M.D., Boston

Cystinosis, or the Lignac-Fanconi syndrome, is a disease of childhood that is characterized by dwarfism and by the accumulation of cystine crystals within many tissues of the body. Investigation reveals a generalized aminoaciduria and renal tubular dysfunction, which is usually manifest by acidosis, hypokalemia, and impaired water reabsorption. Renal rickets and uremia are frequent late sequelae.

While the disturbance is believed to be a hereditary defect in the utilization of many amino acids, cystine precipitates out, presumably because of its low solubility. The condition is not to be confused with the relatively benign cystinuria which appears to result from a lowered renal threshold (for cystine, lysine, and arginine) and which does not reflect a general disturbance of amino acid metabolism, such as is the case with the cystinosis of children.

The ophthalmologic importance of cystinosis is due to the fact that the crystals of cystine can be frequently seen in the cornea, and occasionally in the conjunctiva, and have such a characteristic appearance and distribution as to be pathognomonic of the condition. The ophthalmologic significance is perhaps heightened by the fact that the opacities, although definite and characteristic, can be easily overlooked unless the eyes are examined closely with good illumination and with sufficient magnification. The affected children usually have no ocular symptoms.

Cystinosis was recognized as a pathologic entity as far back as 1903 (Abderhalden [1]), but its recognition in life is relatively recent. The ophthalmic manifestion of cystinosis dates to 1941 with a report by Bürki [2] of a patient with cystinosis showing crystalline deposits in the cornea and conjunctiva. These were seen during life with the slit-lamp biomicroscope and subsequently post mortem in the cornea, conjunctiva, uvea, and sclera.

Since Bürki's initial description of crystals in the cornea and conjunctiva in cystinosis, approximately 20 cases with ocular manifestations have been reported.* All have been characterized clinically by the presence of a myriad of fine white dots situated predominantly in the anterior corneal stroma of the two eyes. In the cases in which conjunctival biopsies were done, birefringent crystals have been found that were identified as cystine. Bürki, who had the unique opportunity of studying histologically the whole eye, identified the crystals by their shape, by their solubility in water and alkali and insolubility in lipid solvents, and by their sulfur content. While little has been added to Bürki's conclusions, his identification of the crystals as cystine has been notably corroborated by means of chromatography (Bickel,[9] 1952) and x-ray diffraction photography (Bickel [9]).

We have had occasion recently to study four cases of cystinosis clinically and to obtain a conjunctival biopsy in one case. While our findings do not greatly enhance the total knowledge on the subject, they do confirm most of the observations already established and contribute a few minor points not heretofore appreciated. All four patients had the dwarfism, generalized aminoaciduria,

Received for publication Oct. 24, 1955.

Howe Laboratory of Ophthalmology, Harvard Medical School, and Massachusetts Eye and Ear Infirmary.

* References 3 to 13.

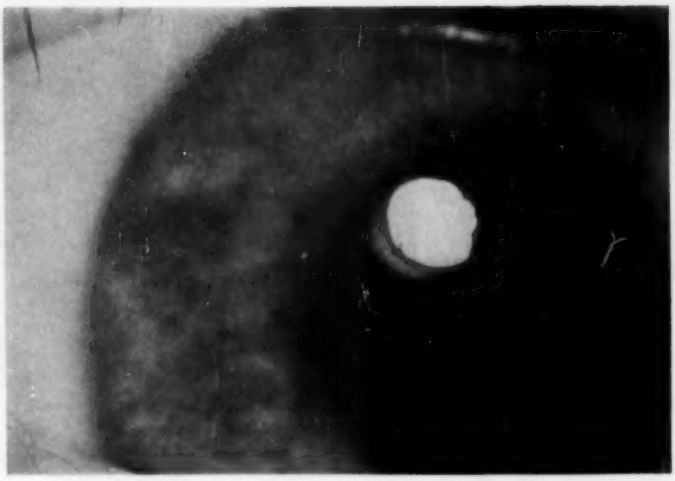


Fig. 1 (Case 1). — Scintillating particles in the cornea evident about the reflection of the flash bulb and representing the appearance as seen with the slit lamp. Although pictured in only a limited area, the particles were actually scattered uniformly over the entire cornea. They could scarcely be seen with the unaided eye and with ordinary flashlight illumination.

and disturbances of water and electrolyte metabolism. None of them had ocular symptoms, and it is to be noted that none had been observed to have corneal opacities or other ocular abnormality on the routine physical examination, even though the eyes had been examined carefully.

REPORT OF CASES

CASE 1.—This patient was studied by the Children's Medical Service of the Massachusetts General Hospital and is being reported in detail by Kelly and Radebaugh.[14]

Four-year-old child who had appeared to be normal until the second year of life, when he did not grow normally and developed an inordinate craving for water and salt. During his third year he developed a microcytic anemia. His referral to the hospital was prompted by an episode of hyperpnea and dehydration.

On admission to the hospital he was found to be an underdeveloped child, extremely irritable, and considerably dehydrated. Significant laboratory studies showed a blood sugar of 150 mg/100 cc. with glycosuria; serum sodium, 146 mEq/l.; serum potassium, 3.3 mEq/l.; CO_2, 14 mEq/l.; chloride, 109 mEq/l.; pH, 7.46, and NPN, 91 mg/100 cc. The α-amino nitrogen of the urine was found to be between 2% and 4.4% of the total urine nitrogen. Urea and creatinine clearances indicated a reduction in glomerular filtration to a level of approximately

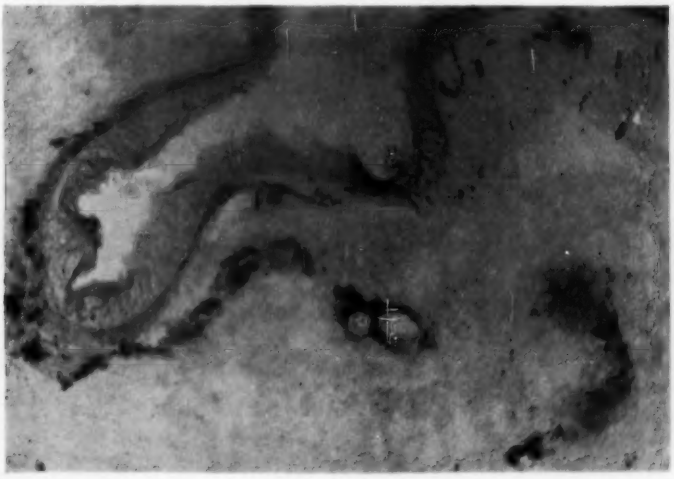


Fig. 2 (Case 1).—Biopsy specimen of conjunctiva cut in frozen state and stained with silver nitrate (von Kossa's stain). With this technique the crystals were blackened and stood out conspicuously.

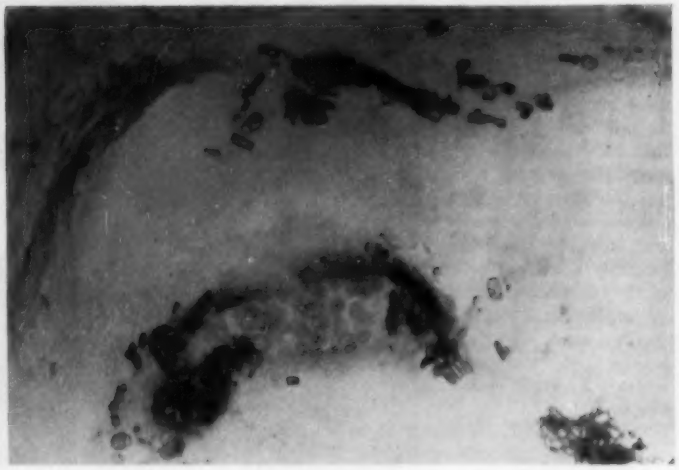


Fig. 3 (Case 1).—High-power magnification section in Figure 2, showing crystals free in the tissue, especially beneath the epithelium, and in the wall of a blood vessel.

7% of normal. These findings were interpreted as indicating chronic uremia. Poor concentration of dye was noted in the intravenous pyelograms, in which demineralization of bone with coarse trabeculae was also observed. A bone marrow biopsy showed no abnormality; but, inasmuch as the tissue was kept for some time in 50% alcohol, the absence of cystine crystals was probably not significant.

Examination of the eyes showed nothing abnormal with ordinary illumination and casual inspection. However, with an intense light and some magnification by a loupe a faint opacity could be seen near the surface of both corneas. There was, nevertheless, no irregularity of the surface. By slit-lamp microscopy a myriad of tinsel-like, slightly yellow opacities could be seen in the immediately subepithelial regions of both corneas. These were most abundant in the pupillary area but extended out to the periphery, where there were also similar opacities in the region immediately in front of the posterior surfaces. The midstromal region was everywhere free of opacities. No abnormalities were seen in the conjunctivas, but, naturally, the cooperation of a 4-year-old child limited the thoroughness of the slit-lamp study.

The corneas were photographed with the Donaldson camera (Fig. 1); and, while the pictures give a true indication of the opacities as seen with the biomicroscope, they suggest that the opacities were more obvious than was actually the case with the unaided eye.

A biopsy of the conjunctiva was obtained from the lower bulbar portion of one eye. Part of the specimen was placed in formalin, and part was sec-

Fig. 4 (Case 1).—Biopsy specimen of conjunctiva, stained with hematoxylin and eosin, showing unstained crystals lying free in the tissues.

tioned in the frozen state and subjected to various staining and experimental procedures. That which was fixed in formalin and sectioned within a few hours showed crystals similar to those found in the fresh-frozen state; however, there was a gradual but complete disappearance of the crystals from the specimen kept in formalin for 24 hours.

Crystals were scattered abundantly throughout the conjunctival stoma. There was some predilection for the subepithelial region and an especial accumulation in the walls of the blood vessels (Figs. 2 and 3). The crystals were predominantly intracellular, but there were also some extracellular crystals singly and in clumps (Fig. 4). The cells containing the crystals appeared to be tissue cells and endothelial cells. There was no tissue reaction. The morphology of the crystals was variable and corresponded to that pictured by Bürki, with a predominance of rectangular forms of various sizes up to 20μ. Hexagonal crystals were, however, common. Many, and probably most, of the larger crystals were birefringent. The crystals were colorless and took none of the ordinary stains (hematoxylin and eosin, Sudan, Nile blue, brilliant green) except for precipitating to some extent the iodine in von Kossa's stain. Thus, they were demarcated most strikingly with this stain.

The crystals were found to be slowly soluble at room temperature in aqueous solution, including 4% solution formaldehyde (U. S. P. XIII), but insoluble in absolute alcohol. In solutions of different hydrogen ion concentrations, they were found to be rapidly soluble in pH ranges greater than 8 and slowly soluble in the range of pH 5-8. With a solution of pH 4 or less the crystals lost their characteristic shape and birefringence and became amorphous material. This change was not reversed by placing the crystals back into a neutral solution.

Cystine crystals added to gelatin and smeared on slides were found to be similarly soluble in alkaline solutions and to lose their crystalline structures in acid solutions.

Chromatographic studies were carried out on the formalin eluate and on the water eluate of several pieces of conjunctiva.

The specimens of conjunctiva were first placed in saline for 15 minutes. This preliminary soaking served to wash out the more soluble components of the tissue but left most of the crystals in situ. These crystals were then dissolved by extracting the tissue with 4% formaldehyde solution U. S. P. XIII, for 18-20 hours. The extract was filtered and then brought to dryness by vacuum distillation. The residue was dissolved in 5 ml. of 1 N HCl and again dried *in vacuo*. This operation was repeated three times to insure complete removal of the formaldehyde. After this procedure, the residue was dissolved in 5 ml. of water and dried *in vacuo* to remove the HCl. Finally, the dried material was dissolved in 0.1 ml. of 0.1 N HCl and the solution concentrated to about 10μl-20μl. This concentrate was spotted on Whatman filter paper #1 for chromatographic studies. Formaldehyde extracts were prepared from two separate pieces of the conjunctiva. One extract was chromatographed, using phenol saturated with water as the solvent system, while the other extract was analyzed on the chromatogram using 70% ethanol-30% 1 N NH_3. The paper chromatograms were allowed to develop in an ascending direction for 12-18 hours, then dried and sprayed with 2% alcohol solution of ninhydrin to locate the position of the unknown compound and reference amino acids. Aminoacetic acid, glutamic acid, cystine, and tyrosine served as reference points on the chromatogram. For a tissue control, a specimen of conjunctiva was removed from a normal subject and was treated in the manner described above.

The chromatographic results, summarized in the accompanying Table, indicate that the extract of

Chromatographic Studies of Conjunctiva Extract

	R_F Values	
	Phenol-Water	Ethanol-NH_3
Extract of conjunctiva with crystals	0.23	0.42
Cystine	0.21	0.41
Aminoacetic acid	0.51	0.59
Glutamic acid	0.34	0.55
Tyrosine	0.62	....

the conjunctiva with the crystals yielded one definite ninhydrin-reactive material with R_F values corresponding to cystine in both solvent systems. The fact that the unknown compound migrated to the same position as cystine in two different solvent systems indicated that these compounds are identical. The appearance of only one ninhydrin spot in the chromatogram suggested that other amino acids were not precipitated in the tissue or that they were lost in the preliminary washing procedure. The extract of the conjunctiva which served as a tissue control did not give any ninhydrin spots.

Case 2.—This case was studied by the Metabolism Division of the Children's Medical Center of Boston.†

Three-year-old boy who was admitted to the hospital for study of an obscure kidney disease.

† Dr. J. Metcoff supervised the metabolic studies on this and on the subsequent patients in this series. He will make a more detailed report of the findings elsewhere (Metcoff, J.; Ring, H.; Satijabrata, K., and Craig, J.: Cystine Storage Disease, to be published).

The patient had developed normally until the age of 2 years, when he gradually developed excessive thirst and polyuria with retardation in his rate of growth. He was first hospitalized in Canada for an acute febrile illness with vomiting and extensive dehydration, and was found to have a urinary specific gravity of less than 1.010. Consequently, a diagnosis of diabetes insipidus was made and he was treated with vasopressin injection (Pitressin); this produced no change in urinary concentration or volume of urine flow. A noteworthy chemical abnormality of the serum was a potassium of only 2.0 mEq/l. following parenteral potassium therapy.

Physical examination on admission showed moderate dwarfing but no dehydration or other significant abnormality. Among other things, metabolic studies showed the following: (1) an abnormally elevated daily water turnover; (2) no increase in urinary concentration in response to intravenous vasopressin; (3) inability to conserve potassium when on a restricted potassium intake; (4) increase of α-amino nitrogens in urine to approximately five times the normal, with wide spectrum of amino acids evident in paper chromatography, and (5) crystals in the interstices of kidney tissue obtained for biopsy, with extensive degenerative changes in the kidney tubules but sparing of the glomeruli, save for slight thickening of the basement membrane.

The eyes showed nothing abnormal on superficial gross observation. With a strong focal light and a magnifying loupe, however, a faint diffuse opacification of the cornea could be made out. With the slit-lamp biomicroscope the corneal surface was smooth, but immediately beneath the surface was a myriad of reflectile particles, simulating Christmas tinsel. These were symmetric in the two eyes, were distributed uniformly over the entire cornea, and extended into the conjunctiva, but spared an irregular area in the approximate center of each cornea. These clear zones approximated one-half the pupillary area when the pupil was 4 mm. in diameter. With the fine beam of the slit lamp these opacities were seen to be situated entirely in the anterior-most stroma.

Case 3.—This case was studied by the Metabolism Division of Children's Medical Center of Boston.

Four-year-old boy who was admitted to the hospital for study. Since the age of 2 years he had been carefully observed for a potassium-losing syndrome, since his brother had been known to have such a disease. However, the patient was apparently well until the age of 3 years, when he had a febrile episode and rash that was diagnosed as scarlet fever. Shortly thereafter he developed generalized weakness, weight loss, and albuminuria with low blood potassium. The EKG showed the characteristic changes of hypokalemia. He was given potassium acetate, and muscular strength improved. He was recalled at this time for study, at the request of the Metabolic Division. His older brother had previously been studied by this Division for a disorder characterized by dwarfing, rickets, disturbance of acid-base regulation, and an electrolyte disorder in which hypokalemia was the outstanding feature. The renal function of this patient was impaired markedly, and he died in uremia at age 6. Cystine crystals were found in many of the tissues when the autopsy material was reviewed, once the diagnosis was established.

Examination at the time of admission revealed some dwarfing, albuminuria, and an NPN of 40 mg/100 cc., but nothing else of significance on routine tests. The child had been on high-potassium, high-alkali intake at home and consequently was in good acid-base and electrolyte balance. X-rays showed mild osteoporosis but no rickets. Special studies revealed moderate ability to conserve potassium on potassium-deficient diets, a good response to vasopressin, an elevation of the α-amino nitrogen levels in the urine, attributed by chromatography to many amino acids, and normal dextrose tolerance tests. A renal biopsy showed slight degeneration in the renal tubules with minimal thickening of the basement membrane of the glomeruli, and crystals in the interstitial tissue.

Examination of the eyes showed nothing abnormal by casual inspection, but with good focal illumination there was a faint haze throughout the entire extent of both corneas. With slit-lamp biomicroscopy this opacity was seen to be made up of numerous scintillating and discrete opacities situated predominantly in the most superficial stroma, immediately beneath the epithelium. These extended uniformly throughout the entire cornea, even to the limbus, and were symmetric in the two eyes. At the periphery there were a few similar crystalloid opacities in front of the posterior surface. The midstroma, however, was everywhere free of opacities.

Case 4.—This case was studied by the Metabolism Division of the Children's Medical Center of Boston.

Three-year-old boy who was studied for an undiagnosed kidney condition (salt-losing nephritis). He had been hospitalized one year previously for polyuria, polydipsia, and dwarfism. His maximum urinary specific gravity was 1.010 and did not rise in response to vasopressin. He had generalized hypoelectrolytemia with a potassium level of 2.9 mEq/l. There were some albuminuria, a normal NPN, and normal intravenous pyelograms. Bone films showed minimal osteoporosis. The most striking abnormality was the finding of a urinary α-amino nitrogen level of 252 mg. in 24 hours, which is over 10 times the normal.

A recent physical examination showed generalized dwarfing but no evidence of rickets or other

abnormality. Bone-marrow biopsy showed large numbers of crystals.

Examination of the eyes showed nothing abnormal with gross inspection, but slit-lamp biomicroscopy revealed a myriad of scintillating particles just beneath the anterior surface, extending to and involving the limbal region of both corneas. These were symmetric in the two eyes. They were also present, although less visible, against the white background in the conjunctivas.

COMMENT AND CONCLUSIONS

The biomicroscopic findings in the cornea are pathognomonic of the disease. In no other condition of which we are aware is there the uniform deposition of scintillating particles situated preferentially beneath the anterior surface (and, to a less extent, in front of the posterior surface at the corneal periphery). So characteristic are these findings that biopsy studies would seem to be unnecessary for the diagnosis.

While unequivocal and striking with biomicroscopy, the corneal opacities are so inconspicuous by gross examination as to be readily overlooked.

We have no firm hypothesis to account for the preferred localization of the crystals in relation to the surfaces of the cornea. One possibility is that these regions, representing the sites where water is selectively removed, induce a local supersaturation and consequent precipitation of the cystine. Such an explanation has previously been suggested to account for the localization of band keratopathy with hypercalcemia.[16] Another possibility, without, as yet, any foundation in fact, is that the oxidation-reduction potential of the cornea in these regions is such as to maintain the cystine in an oxidized, and therefore relatively insoluble, form.

In the conjunctiva the crystals are aggregated preferentially, but not exclusively, in the walls of the blood vessels. This suggests a participation of the reticuloendothelial system but does not necessarily indicate phagocytosis.

243 Charles St. (14).

REFERENCES

1. Abderhalden, E.: Familiäre Cystindiathesis, Ztschr. physiol. Chem. **38**:557, 1903.

2. Bürki, E.: Über die Cystinkrankheit im Kleinkindesalter unter besonderer Berücksichtigung des Augenbefundes, Ophthalmologica **101**:257, 1941.

3. Streiff, E. B.: Altérations de la cornée chez les enfants en bas age (keratomalacie; dépots de cystine), Bull. mém. Soc. franç. opht. **61**:160, 1947.

4. Müller, H. K.: Über die Bedeutung von Augenveränderungen für die Diagnose der Zystinkrankheit im Kindesalter, Klin. Monatsbl. Augenh. **119**:205, 1951.

5. Douglas, A. A.: A Case of Syndrome of Fanconi, Tr. Ophth. Soc. U. Kingdom **70**:98, 1950.

6. Ullerich, K.: Über Augenveränderungen bei der Cystinkrankheit, Ber. deutsch. ophth. Gesellsch. **57**:306, 1951.

7. Brændstrup, P.: Infantile Cystinosis with Cystine Crystals in Cornea and Conjunctiva, Acta ophth. **30**:365, 1952.

8. Kennedy, J. A.: Cystinosis with Crystal Deposits in the Cornea and Conjunctiva, Am. J. Ophth. **35**:1596, 1952.

9. Bickel, H., and others: Cystine Storage Disease with Aminoaciduria and Dwarfism, Acta pædiat. **42** (Supp. 90), 1952.

10. Guild, H. G.; Walsh, F. R., and Hoover, R. E.: Ocular Cystinosis, Am. J. Ophth. **35**:1241, 1952.

11. Goar, E. L., and De La Motte, G. W.: Cystine Crystals in the Cornea and Conjunctiva, A. M. A. Arch. Ophth. **51**:336, 1954.

12. Bürki, E.: Ein weiterer Fall von Cystinosis mit Hornhaut veränderungen, Ophthalmologica **127**:309, 1954.

13. Thomas, C.; Cordier, J., and Algon, B.: Contribution ophthalmologique du diagnostic der nanismes: la cystinose de la cornée, Bull. Soc. opht. France, p. 546, 1954.

14. Kelly, E., and Radebaugh, J.: Cystine Storage Disease, J. Maine M. A., to be published.

16. Cogan, D. G.; Albright, F., and Bartter, F. C.: Hypercalcemia and Band Keratopathy: Report of 19 Cases, Arch. Ophth. **40**:624, 1948.

Sarcoidosis of the Lacrimal Glands Associated with Sjögren's Syndrome

Their Relationship with Mikulicz' Syndrome

CAPT. ELLIS GRUBER (MC), U. S. A. F.

Generalized sarcoidosis is now recognized as a fairly common disease, and much has been written about it in recent years. However, in a review of the literature, it is apparent that sarcoidosis of the lacrimal glands as the only evidence of ocular involvement is fairly rare, and this case is probably the first to be reported in which Sjögren's syndrome was present in the same patient.

SARCOIDOSIS

It was Boeck,[1] in 1899, who first described sarcoid of the skin. This is the commonest type of sarcoid that is found. In 1904 Darier and Roussy [2] first described a different type of sarcoid from Boeck's, in that it was subcutaneous rather than in the skin, and it was a rare variety occurring essentially in the extremities. As for sarcoidosis of the lacrimal glands, Wexler,[3] in 1939, presented a case of bilateral swelling of the lacrimal glands in a Negro aged 29. In the same year, Walsh,[4] in his paper, described a case of bilateral swelling of the lacrimal glands as the only eye sign in widespread sarcoidosis affecting the skin in a Negro woman aged 38. He stated that spontaneous resolution often indicates the diagnosis. Two years later, Rosenbaum [5] reported a case of bilateral swelling of the lacrimal glands in a white woman aged 26 who had no other eye signs. Cullom and Goodpasture [6] also reported a case of bilateral swelling of the lacrimal glands in a Negro woman aged 24. Sniderman [7] reported a similar case, but this was also associated with a bilateral iridocyclitis, and he stated that lacrimal gland involvement was extremely rare. Stallard [8] described a case of sarcoidosis of just one lacrimal gland, which was confirmed microscopically. Many other ocular changes can occur in this disease, as was well described by Levitt.[9] Usually when the lacrimal glands are enlarged, so also are the salivary glands, forming what is known as Mikulicz' "disease." If there is a uveitis also, this may then be called uveoparotid fever (Heerfordt's disease). But doubtless these are all variations of the same disease process.

The typical histological picture shows small nodules of epithelioid cells, which never show caseation or necrosis. Some lymphocytes may be present around the nodules, and there may be a few giant cells also, which sometimes contain small refractile bodies. Healing usually occurs by fibrosis.

SJÖGREN'S SYNDROME

This condition was first described by Sjögren [10] in 1933. He recorded 19 cases, all female and mostly menopausal. Duke-Elder [11] describes it thus:

> A failure in lacrimal secretion associated with an atrophic and cirrhotic condition of the lacrimal glands occurring as part of a general systemic disturbance of unknown origin is a somewhat rare condition met with usually in women after the menopause, giving rise to symptoms of keratoconjunctivitis sicca; it is typically accompanied by a similar failure of the secretion of the salivary and mucous glands of the upper respiratory tract, and frequently by polyarthritis.

Raffle,[12] in his article, stated that the ocular features may be delayed, and his case of Sjögren's disease had no eye signs or symptoms at all.

Received for publication Sept. 21, 1955.

Gifford and associates[13] divided their 49 cases of keratoconjunctivitis sicca into three groups. The first group comprised 16 patients who showed a lacrimal deficiency with moistening of less than 15 mm. on the Schirmer test after five minutes, but no corneal or associated changes. The case report which is to follow falls into this group. The typical histological picture of the lacrimal gland shows an extensive round-cell infiltration of lymphocytes and plasma cells, connective tissue proliferation, and eventually fibrosis. The glands become small and cirrhotic, showing an almost complete degeneration and atrophy of their parenchymatous elements. The parotid glands usually show a lymphoid infiltration and atrophy, as do the mucous glands of the upper respiratory tract.

MIKULICZ' "DISEASE"

This condition is a chronic painless swelling of the lacrimal and salivary glands, usually bilateral. It need not affect both glands, and it affects the salivary oftener than it does the lacrimal. It was first described by Mikulicz[14] in 1892. However, since that time it has become apparent that the disease is merely a symptom complex that might be produced by any one of several causes, such as sarcoidosis, lymphoma, leukemia, or tuberculosis. It is probable that many cases that have been diagnosed as Mikulicz' disease were in fact examples of sarcoidosis. The histology shows a lymphoid hyperplasia of the glands with secondary destruction of their parenchyma, and this is not unlike the histological picture of Sjögren's syndrome. One wonders whether some cases diagnosed as Mikulicz' disease could really belong to Sjögren's syndrome.

REPORT OF A CASE

A 50-year-old white woman was first seen in May, 1955, complaining of a painless swelling of both upper eyelids for the last few weeks, which made it hard for her to open her eyes fully. There was some sensitivity to bright light, and also some blurring of vision when looking up from reading. Past history revealed that for the last six years she had noticed difficulty in crying, together with a sensation of dryness of the eyes, mouth, throat, nose, and ears. These symptoms coincided with the onset of her menopause. For this same period of time she had also had rheumatoid arthritis involving her knees, wrists, and shoulders, for which she had been given various medications, without much relief. She had never received any hormone therapy. Her thyroid gland had been enlarged since her early teens, but it had never given her any toxic symptoms. The parotid glands had never been swollen. She had no other complaints and denied any cough, dyspnea, or chest pain. The family history was unremarkable.

Eye examination revealed a swelling of both upper lids, particularly in the outer aspects. Over the area of both lacrimal glands could be felt a firm, nodular, nontender mass, about 1×2 cm. in size, which was freely mobile and not attached to the skin or bone. The upper limits went up under the roof of the orbit and could not be felt. There was no displacement of the globe and no interference with ocular motility. The vision was correctable to 20/15 in each eye. The lids, conjunctivae, corneae, A. C.'s, irides, and pupils were normal, as were the media and fundi. There was no evidence of any conjunctival secretion. Slit-lamp examination of both eyes was entirely negative, but on staining with fluorescein there were two very small superficial staining areas on the right cornea. A Schirmer test revealed a wetting of 8 mm. on the right side and 13 mm. on the left side after five minutes. The salivary glands were not enlarged. The axillary glands were palpable but not the cervical glands. The thyroid gland was diffusely enlarged.

On the basis of these findings, she was admitted to the hospital for a complete work-up. Blood pressure was 105/75. The heart sounds were normal, and the lungs were clear to percussion and auscultation. The liver, kidneys, and spleen were not palpable, and there were no abnormal masses felt in the abdomen. There were two small subcutaneous nodules present over the deltoid region of the left arm, and a similar nodule in the same area of the right arm. These were firm, mobile, and nontender. Flexion of the knees and wrists was slightly limited, and there was a fusiform swelling of the interphalangeal joint of the first digit of each hand. The laboratory findings were as follows:

Hemoglobin 14.3 gm. per 100 cc.; R. B. C. 4,750,000; W. B. C. 6100; differential, 60% polymorphs, 23% lymphocytes, 7% eosinophiles, 6% monocytes, 1% basophiles, and 3% stab forms.

Urinalysis was negative; blood serology was negative.

The sedimentation rate was 35 mm. in one hour (Westergren; normal, 0-20 mm.). Prothrombin time, 16 seconds (normal 15 seconds). Blood cholesterol, 235 mg. per 100 cc. Fasting blood sugar 86 mg. per 100 cc. N. P. N. 33 mg. per

Fig. 1.—X-ray of the chest at the time of admission to the hospital, showing the bilateral hilar adenopathy and the extensive fine fibrosis over both lower lungs.

100 cc. Total protein 6.6 gm., albumin 3.6 gm., globulin 3 gm., per 100 cc. A/G ratio 1.2:1.

The ECG was normal.

X-ray of the chest revealed a bilateral hilar adenopathy, with extensive fine fibrosis throughout the lower two-thirds of both lung fields (Fig. 1). These findings are compatible with the diagnosis of sarcoidosis. X-ray of the right hand and wrist showed a normal mineral content of all the bones except for a small area of aseptic necrosis in the capitate.

The tuberculin skin test (1:1000) was negative.

The two nodules in the left arm were removed for biopsy. Grossly they had the appearance of lipomata.

Microscopic Report (L. W. Gardner, M.D.).—Sections consist of a cutaneous biopsy specimen, covered on the outer aspect by quiescent squamous epithelium showing a slight degree of keratosis. The epithelium is intact, and no evidence of atypical epithelial proliferation is noted. The appendages of the skin hair follicles, sebaceous glands, and sweat glands fail to disclose histopathological change. The upper and middle corium is essentially normal. The lower corium and subcutaneous tissues are the site of a granulomatous process characterized by single and coalescing tubercles. These lesions consist of proliferating epithelioid cells in a concentric arrangement. Some contain a central Langhan's giant cell, while this cell is not present in other tubercles. Careful examination failed to disclose the doubly refractile inclusion bodies occasionally seen in sarcoidosis. Total absence of caseation is conspicuous. The edges of the tubercles contain a few lymphocytes. Acid-fast stains failed to disclose tubercle bacilli.

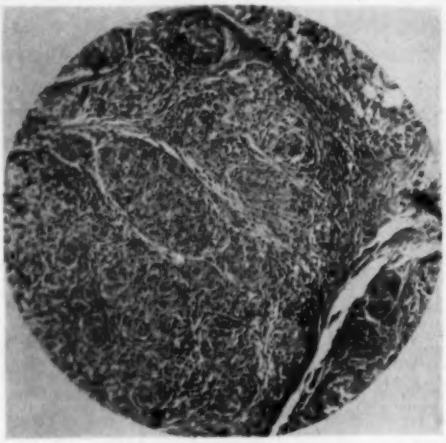
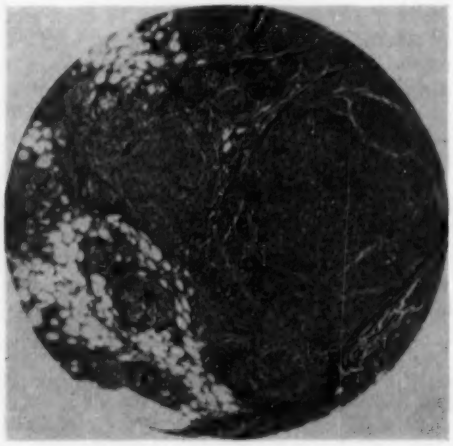


Fig. 3.—Higher power of Figure 2, showing the sarcoid nature in more detail, and also a typical giant cell at the top. Reduced to 57% of mag. × 130.

Fig. 2.—Photomicrograph of the section of the subcutaneous nodule, showing the nodules of concentric epithelioid cells with some lymphocytes around them. Reduced to 72% of mag. ×60.



Diagnosis.—Subcutaneous sarcoid of Darier-Roussy (Figs. 2 and 3).

The differentiation from Boeck's sarcoid is just one of location. In Boeck's sarcoid the epithelioid cells are predominantly in the corium, while in the Darier-Roussy type they are found mainly in the subcutaneous tissue.

Course.—The patient was discharged from the hospital and put on treatment with prednisone (Meticorten). This is a new synthetic corticosteroid, which is more potent than cortisone and has fewer side-effects. She was given 5 mg. tablets to take orally four times a day for a week. This dosage was gradually reduced until a maintenance dose of 5 mg. twice daily was being taken. The lacrimal gland swellings showed an almost immediate improvement; and when she was last seen, the left gland could not be felt at all and the right one was only just palpable. The nodule in the right upper arm had disappeared completely. The arthritis had also improved greatly, and she stated that for the first time in years she was able to run to catch a bus, and that most of the pain in her joints had gone. The dryness in her eyes, mouth, nose, and ears felt much better. She had been able to sneeze, and there was some wax present in her ears for the first time in the last six years. A repeat of the chest x-ray 10 weeks later showed a slight decrease in the bilateral hilar adenopathy, and the extensive fine fibrosis throughout the lower two-thirds of both lungs was not as marked as at the previous examination (Fig. 4). Of course, the diagnosis of sarcoidosis of the lacrimal glands is clinical only. A conclusive diagnosis could only be made by a histological examination of the gland.

Fig. 4.—X-ray of the chest 10 weeks later, showing a decrease in the hilar adenopathy and in the fine fibrosis throughout the lungs.

COMMENT

Sarcoidosis is of great interest because it often involves the eye, and the disease may first be seen by the ophthalmologist. It usually starts in early adult life, and its progress is insidious, until it produces obvious changes. It is said to be commoner in the Negro race, in the proportion 6:1. It commonly affects the skin, bones, lymph nodes, lungs, and eyes, and can affect almost any tissue in the body. It may occur in almost any structure in the eye or ocular adnexa, but the uveal tract is the part most commonly affected, in the form of a granulomatous iridocyclitis. The plasma globulin is often increased and the A/G ratio reversed. An increased sedimentation rate is common, and a slight eosinophilia sometimes occurs. There is a state of anergy to tuberculosis, which means that a patient with sarcoidosis fails to react to tuberculin skin tests, whereas a normal person might. The etiology is unknown, but most investigators believe the disease is the result of an attenuated expression of tuberculosis, being a manifestation of a high degree of immunity with a low degree of allergy. In a study of 35 cases of sarcoidosis, Reisner [15] found that one-third showed a regressive course with apparent recovery. He stated that transition into ordinary tuberculosis apparently represents a potential development in the course of sarcoidosis. Numerous forms of treatment have been tried, but since spontaneous regression is a frequent occurrence, it is difficult to evaluate the beneficial effects of any particular therapy. It is quite possible that the lacrimal gland swelling in the case reported here would have regressed without any treatment. However, the corticosteroid hormones do seem to offer the best form of therapy at the present time.

Although deficient lacrimation is essential in the typical Sjögren syndrome, absence of moisture in the eyes is not as a rule apparent on inspection. Schirmer [16] considered less than 15 mm. wetting in five minutes as abnormal. The failure in secretion of the lacrimal and salivary glands, together with the mucous glands of the upper respiratory

tract, leads to dryness of the eyes, mouth, pharynx, larynx, nose, and sinuses. This represents the complete syndrome, but usually the syndrome is incomplete and limited to one or more of these structures. The sedimentation rate is often increased, and there may be an eosinophilia. Polyarthritis, of the rheumatoid type, is said to occur in 60% of cases. Although most people are of the belief that in Sjögren's syndrome there is never enlargement of the lacrimal glands, and this is almost always true, yet the lymphocytic infiltration that occurs in the early stages of the disease may certainly produce an enlargement. This was stated by Cardell and Gurling,[17] who reported the postmortem findings in three patients with Sjögren's syndrome. Eventually the infiltration disappears and is replaced by fibroadipose tissue and the glands become small. The etiology is unknown, but one of the commonest concepts is that it is due to a glandular dyscrasia. Ellman and Parkes Weber[18] reported a case of Sjögren's disease with an uncertain lung lesion, which in some ways was similar to the case just described. They themselves questioned the lung condition as being of a sarcoid nature, but then they dismissed the idea as being very unlikely. The case was in a woman, aged 34, who had previously had parotid and submaxillary gland swellings, and now had dryness of the mouth and eyes, dry pleurisy, and rheumatoid arthritis. There were diminished air entry at the bases of both lungs and dry crepitations. X-ray of the chest showed a diminished translucency in the left lower lobe, and a repeat x-ray later showed consolidation in this area, and also scattered opacities in the right lower lobe. It would seem that the lung lesion in their case could well have been due to sarcoidosis, if a similarity is to be assumed with the case presented here. They considered Sjögren's disease as a lymphoid granulomatous condition affecting especially the salivary and lacrimal glands, and they therefore wondered whether Mikulicz' disease, which has the same pathology, was allied to, or a variant of, Sjögren's disease. Morgan and Castleman,[19] in an interesting paper on Mikulicz' disease, expressed the same idea. They said it seemed likely that the disease was not a distinct entity, but merely one manifestation of a more generalized symptom complex known as Sjögren's syndrome. Morgan,[20] just more than one year ago, reviewed Sjögren's original microscopic material and found that the pathological changes in the sections of the salivary glands were identical with those previously recorded in 18 cases of Mikulicz' disease. Of these latter 18 patients, 9 showed one or more of the other features found in Sjögren's syndrome, in addition to the disease of the salivary glands. It does seem true that there is a definite relationship between Mikulicz' syndrome and Sjögren's syndrome. They both occur mainly in women past 40 years of age, and they both show a marked similarity in their clinical and pathological aspects. This can also be said for Mikulicz' syndrome and sarcoidosis, as has been mentioned earlier, in that sarcoidosis may be the cause of Mikulicz' syndrome, and they may both have a similar pathological picture. It seems, therefore, that there must be a relationship between sarcoidosis and Sjögren's syndrome, especially as they are coexistent in the case described here. The case presents several factors which are common to both diseases; namely, the patient was a woman more than 40 years old, with an increased sedimentation rate, a slight eosinophilia, dryness of the eyes and mouth, lacrimal gland swelling, and regression of the symptoms with the use of prednisone. All of these features could just as well fit in with the diagnosis of sarcoidosis as with the diagnosis of Sjögren's syndrome. The fact that these two diseases have so many features in common surely points to their being directly related to each other. Another interesting factor in this case is the enlargement of the thyroid gland. This condition could fit in very well with Hashimoto's type of chronic thyroiditis. This also occurs as a rule in women past 40, and the gland shows an extensive lymphoid infiltration, with maybe some giant cells and atrophy of the gland parenchyma and fibrosis. This is the

same picture as that seen in Sjögren's syndrome. The etiology is unknown, but the disease could well be part of this same symptom complex.

In conclusion, it would appear that in considering sarcoidosis, Sjögren's syndrome, and Mikulicz' syndrome (and possibly Hashimoto's thyroiditis) we are dealing with parts of one large syndrome caused by the same disease process. The etiology of them all remains obscure, despite the numerous theories. They are all systemic diseases, and it is likely that they have a common etiological factor, probably infective in nature, and possibly due to a virus. Grüter [21] showed that there is a virus capable of producing changes like those of keratoconjunctivitis sicca when introduced into the eyes of animals, and this virus normally inhabits the mouth and nasopharynx. In favor of an infective process is the fact that pathologically they all show a chronic inflammatory reaction; also, in sarcoidosis there is the increased sedimentation rate and increased globulin, and in Sjögren's syndrome there is the increased sedimentation rate and the polyarthritis.

SUMMARY

An unusual case is presented showing generalized sarcoidosis with bilateral swelling of the lacrimal glands, together with Sjögren's syndrome. Treatment with prednisone (Meticorten), a new corticosteroid, gave relief of both conditions. The literature is reviewed, and the signs and symptoms occurring in sarcoidosis, Sjögren's syndrome, and Mikulicz' syndrome are discussed, together with their histological features. It is suggested that there is a definite relationship of all three diseases, and that there is probably a common etiological factor of a chronic infective nature.

3650th U. S. A. F. Hospital, Sampson Air Force Base, Geneva, N. Y.

REFERENCES

1. Boeck, C.: Multiple Benign Sarcoid of the Skin, J. Cutan. Dis. **17**:543, 1899.

2. Darier, J., and Roussy, G.: Un Cas de tumeurs bénignes multiples (sarcoides sous-cutanées ou tuberculides nodulares hypodermiques), Ann. dermat. et syph. **5**:144, 1904.

3. Wexler, D.: Sarcoid of the Lacrimal Gland, Arch. Ophth. **23**:220, 1940.

4. Walsh, F. B.: Ocular Importance of Sarcoid, Arch. Ophth. **21**:421, 1939.

5. Rosenbaum, J.: Boeck's Sarcoid of the Lacrimal Gland, Arch. Ophth. **25**:477, 1941.

6. Cullom, M. M., and Goodpasture, E. W.: Boeck's Sarcoid: A Case of Bilateral Tumor of the Lacrimal Gland, Arch. Ophth. **26**:57, 1941.

7. Sniderman, H. R.: Boeck's Sarcoid of the Lacrimal Gland with Bilateral Iridocyclitis, Am. J. Ophth. **24**:675, 1941.

8. Stallard, H. B.: Boeck's Sarcoidosis of the Lacrimal Gland, Brit. J. Ophth. **24**:451, 1940.

9. Levitt, J. M.: Boeck's Sarcoid with Ocular Localization, Arch. Ophth. **26**:358, 1941.

10. Sjögren, H.: Zur Kenntnis der Keratoconjunctivitis Sicca, Acta ophth., Supp. 2, 1933.

11. Duke-Elder, S. W.: Text-Book of Ophthalmology, Vol. V, St. Louis, C. V. Mosby Company, 1952, p. 5236.

12. Raffle, R. B.: Sjögren's Disease Associated with a Nutritional Deficiency Syndrome, Brit. M. J. **1**:1470, 1950.

13. Gifford, S. R.; Puntenney, I., and Bellows, J.: Keratoconjunctivitis Sicca, Arch Ophth. **30**: 207, 1943.

14. Mikulicz, J.: Über eine eigenartige symmetrische Erkrankung der Thränen und Mundspeicheldrüsen, Beitr. Chir. Festschr. Theodor Billroth, Stuttgart, F. Enke, 1892, p. 610.

15. Reisner, D.: Boeck's Sarcoid and Systemic Sarcoidosis, Am. Rev. Tuberc. **49**:437, 1944.

16. Schirmer, O.: Studien zur Physiologie und Pathologie der Tränenabsonderung und Tränenabfuhr, von Graefes Arch. Ophth. **56**:197, 1903.

17. Cardell, B. S., and Gurling, K. J.: Observations on the Pathology of Sjögren's Syndrome, J. Path. & Bact. **68**:137, 1954.

18. Ellman, P., and Parkes Weber, F.: Sjögren's Disease, with Dryness of the Bronchial Mucosa and Uncertain Lung Lesion, Brit. M. J. **1**:304, 1949.

19. Morgan, W. S., and Castleman, B.: A Clinicopathologic Study of "Mikulicz's Disease," Am. J. Path. **29**:471, 1953.

20. Morgan, W. S.: The Probable Systemic Nature of Mikulicz's Disease and Its Relation to Sjögren's Syndrome, New England J. Med. **251**: 5, 1954.

21. Grüter, W.: Las Enfermedades herpeticas oculares a la luz de las modernas investigaciones del virus, Arch. Soc. oftal. hispano-am. **3**:494, 1943.

Influence of Low-Voltage X-Radiation on Regression of Established Corneal Vessels

I. C. MICHAELSON, Jerusalem
and
H. SCHREIBER, Haifa

It has been shown experimentally that low-voltage x-radiation in appropriate doses can inhibit new-vessel growth into the cornea (Scheie and associates,[3] 1950; Michaelson and associates,[2] 1954). Experimental work has shown that such x-radiation fails to prevent new-vessel growth (Michaelson and associates, 1954). In the inhibition experiments the radiation was given shortly after commencement of active neovascularization. In the prevention experiments the radiation was given some time before the onset of the experimentally produced vascularization or coincidentally with its onset. Reports on the regression effect of radiation on experimentally produced vascularization are not available. By this is meant the effect of the radiation on established corneal vessels after the factor stimulating the presence of these vessels has ceased to be operative. It is of some practical importance to know whether such a regressive influence exists in order, for example, to know whether it is worth while radiating a vascularized cornea prior to corneal grafting.

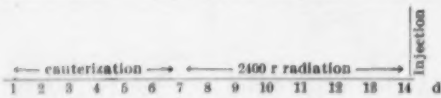
Received for publication Sept. 12, 1955.

MATERIAL AND METHOD

The method of producing and measuring corneal vascularization has already been described (Campbell and Michaelson,[1] 1949). A standard thermal lesion was produced in both corneae of rabbits of about 1.5 kg. weight. The lesion was made by means of an electrocautery applied about 2.5 mm. from the limbus in the 12 o'clock meridian. An attempt to standardize the lesion was made by supplying the cautery with a fixed voltage and applying it for a fixed time. The cautery was reapplied to the wound daily for a certain number of days during the course of each experiment.

With the aid of a Phillips low-voltage contact therapy machine, using 50 kv. and 2 ma., x-rays were applied to the upper portion of the cornea of the right eyes of all the animals, the area irradiated

TABLE 1.—*Effect of 2400 r of X-Radiation Given During Week Following Completion of Vascularization.**



Rabbit No.	Left Eyes (Not Irradiated)		Right Eyes (Irradiated)	
	Wound-Limbus Distance, Mm.	Area of Vasc. Sq. Mm.	Wound-Limbus Distance, Mm.	Area of Vasc. Sq. Mm.
152	2.5	13.5	2.0	9.0
154	2.5	13.5	2.5	12.0
155	2.4	13.5	2.0	14.7
156	2.0	12.5	2.5	11.9
157	2.5	13.1	2.0	11.0
158	2.4	11.7	1.9	13.0

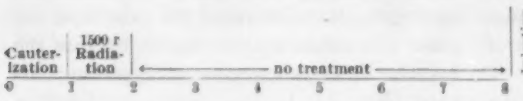
* The India-ink injections were made immediately after completion of radiation.

The wounds were all between 1.25 and 1.75 mm. in diameter.

The mean of the wound-limbal distances in the left eyes was 2.4 mm. (range 2.0-2.5 mm.); the mean of the wound-limbal distances in the right eyes was 2.1 mm. (range 1.9-2.5 mm.).

The mean of the vascular areas in the left eyes was 12.9 sq. mm. (range 11.7-13.5 sq. mm.); the mean of the vascular areas in the right eyes was 11.9 sq. mm. (range 9.0-14.7 sq. mm.). There is no significant difference between the areas of vascularization produced in the treated and the untreated eyes.

TABLE 2.—*Effect of 2400 r of X-Radiation Given During Week Following Completion of Vascularization* *



Rabbit No.	Left Eyes (Not Irradiated)		Right Eyes (Irradiated)	
	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.
200	2.8	0.6	2.6	0.6
201	2.8	0.2	2.8	0.9
202	3.0	0.6	2.8	2.2
203	2.8	No vessels	Wound not discernible	1.3
204	2.8	0.6	2.8	2.2
205	2.6	No vessels	2.8	0.4
206	2.8	0.4	2.9	1.7
207	2.2	0.6	2.8	0.9
208	2.2	0.6	2.1	1.7
209	2.8	0.3	3.0	0.6

* The India-ink injections were made six weeks after completion of radiation.
The wound diameters were all between 1.25 and 1.75 mm.
The mean of wound-limbal distances in the left eyes was 2.7 mm. (range 2.2-3.0 mm.); the mean of wound-limbal distances in the right eyes was 2.7 mm. (range 2.1-3.0 mm.).
The mean of the heights of the vascular areas in the left eyes was 0.4 mm. (range 0.0-0.6 mm.); the mean of the right eyes was 1.3 mm. (range 0.4-2.2 mm.).

extending from the wound to the limbus, and therefore including the vascularized portion of the cornea. Exposures were given through a 15 mm. aperture. The left eyes were used as controls.

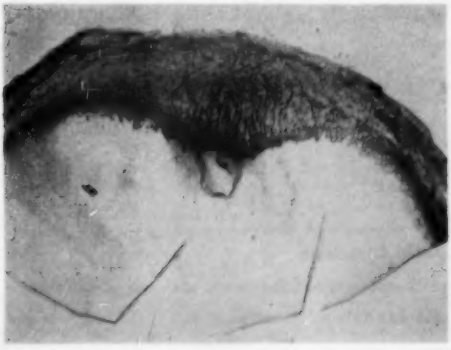
In one series of experiments the radiation (2400 r) was applied for seven days after the production of the vascularization had ceased. At the end of this period the animals were injected and the vascularization extents measured.

In a second series of experiments a similar procedure was carried out, using 2400 r of radiation, but the injection of the animals was deferred until six weeks after the irradiations had been completed.

In these experiments it was apparently clear that (1) a waiting period of six weeks did not apparently affect the result, and (2) the dose of 2400 r was not effective in regressing the vessel growth, but even appeared to stimulate it.

Third and fourth experiments were therefore carried out in which the doses of radiation were 1500 and 700 r, respectively. The waiting periods after the completion of the radiation in the third and fourth experiments were two to four weeks.

Fig. 1.—Appearance of vascularization in injected Rabbit 152 (right eye).



RESULTS

EXPERIMENT 1.—The results are given in Table 1. The similarities of wound-limbal distances and wound diameters in this experiment, as in the other experiments given in this report, permit comparison of the right and left eyes with regard to the extent of

Fig. 2.—Appearance of vascularization in injected Rabbit 207 (right eye). It is not now possible to estimate the area of vascularization.

vascularization produced. In each animal a satisfactory injection was obtained (Fig. 1). The area of vascularization is calculated from the base and height measurements of the triangular vascular area.

The mean of the vascular areas in the right eyes is 11.9 sq. mm. (range 11.7-13.5 sq. mm.); the mean of the vascular areas in the left eyes is 12.9 sq. mm. There is no significant difference between the areas of vascularization produced in the irradiated and nonirradiated eyes.

EXPERIMENT 2.—The results are shown in Table 2. After a certain period it is often most difficult to determine the extents of the areas of vascularization present because the vascular triangle has now a ragged appearance (Fig. 2). In this experiment, and in the subsequent ones, only the height of the vascular area from the limbal base is given. The mean height of the vascular area in the right eyes was 1.4 mm. (range 0.4-2.2 mm.); the mean height in the left eyes was 0.4 mm. (range 0.0-0.6 mm.).

TABLE 3.—*Effect of 1500 r of X-Radiation Given During Week Following Completion of Vascularization* *

Cauterization	1500 r radiation	no treatment	Injection
0	1	2 3 4	weeks

Rabbit No.	Left Eyes (Not Irradiated)		Right Eyes (Irradiated)	
	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.
57	2.5	3.0	2.5	3.0
58	2.5	3.0	—	—
59	2.0	3.0	2.5	3.1
60	2.5	3.0	2.5	3.0
61	2.0	2.8	2.5	3.0
62	2.5	3.0	2.0	2.5
63	2.5	3.2	2.0	2.5
64	—	—	2.4	3.2
65	2.3	3.0	—	—
66	—	—	2.5	3.0
67	—	—	2.3	3.2
68	2.0	3.0	2.0	3.0
69	—	—	2.5	3.3

* The India-ink injections were made two weeks after completion of radiation.
The wounds were all between 1.25 and 1.75 mm. in diameter.
The mean of the wound-limbal distances in the left eyes was 2.3 mm. (range 2.0-2.5 mm.); the mean of the wound-limbal distances in the right eyes was 2.3 mm. (range 2.0-2.5 mm.).
The mean of the heights of the vascular areas in the left eyes was 3.0 (range 2.8-3.2 mm.); the mean for the right eyes was 3.0 mm. (range 2.5-3.3 mm.).

TABLE 4.—*Effect of 700 r of X-Radiation Given During Week Following Completion of Vascularization* *

Cauterization	700 r radiation	← no treatment →	Injection
0	1	2 3 4 5	6 weeks

Rabbit No.	Left Eyes (Not Irradiated)		Right Eyes (Irradiated)	
	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.	Wound-Limbus Distance, Mm.	Height of Vasc., Mm.
212	2.3	2.8	2.2	2.6
216	2.5	3.0	2.5	3.2
217	2.6	2.6	2.6	3.4
221	2.2	2.6	2.0	2.0

* The India-ink injections were made four weeks after completion of radiation.
The wounds were all between 1.25 and 1.75 mm. in diameter.
The mean of the wound-limbal distances in the left eyes was 2.4 mm. (range 2.2-2.5 mm.); the mean of the wound-limbal distances in the right eyes was 2.3 mm. (range 2.0-2.6 mm.).
The mean of the heights of the vascular areas in the left eyes was 2.9 mm. (range 2.6-3.0 mm.); the mean for the right eyes was 2.8 mm. (range 2.0-3.4 mm.).

It is difficult to measure the density of vascularization, but the general appearance of the density of the vascular areas confirmed the height findings that the right eyes were more vascularized than the nonirradiated left eyes.

EXPERIMENT 3.—The results are shown in Table 3. The mean height of the vascular area in the right eyes is 3.0 mm. (range 2.5-3.3 mm.). The mean height in the left eyes is 3.0 mm. (range 2.8-3.2 mm.). There is no significant difference between the right and left eyes.

EXPERIMENT 4.—The results are shown in Table 4. The mean height of the vascular area in the right eyes is 2.8 mm. (range 2.0-3.4 mm.). The mean height in the left eyes is 2.9 mm. (range 2.6-3.0 mm.). There is no significant difference between the right and left eyes.

COMMENT

It would appear that, although inhibition of active vessel growth can be helped in the cornea by low-voltage radiation, these radiations have no effect in causing the regression of established corneal vessels even after a waiting period of several weeks. Indeed, with a dose of 2400 r there seemed to be even some increase in the number and extent of the vessels present.

SUMMARY

Total doses of low-voltage x-radiation varying from 700 to 2400 r have no regressive effect on established corneal vessels.

Hadassah Medical Organization, Box #499.

Miss Eva Lewkowitz gave technical assistance.

This work was supported by a grant from the Arnold Reuben Fight for Sight Fund of the National Council to Combat Blindness, Inc., New York.

REFERENCES

1. Campbell, F. W., and Michaelson, I. C.: Blood Vessel Formation in the Cornea, Brit. J. Ophth. **33**:248, 1949.

2. Michaelson, I. C.; Gluecker, L., and Stieglitz, E.: Influence of Low-Voltage X-Radiation on Inhibition and Prevention of New Vessels in Cornea, A. M. A. Arch. Ophth. **52**:77-84, 1954.

3. Scheie, H. G.; Dennis, R. H.; Ripple, R. C.; Calkins, L. L., and Buessler, J. A.: Effect of Low-Voltage Roentgen Rays on Normal and Vascularized Cornea of Rabbit, Am. J. Ophth. **33**:549, 1950.

The Radioactive Phosphorus (P^{32}) Uptake Test in Ophthalmology

A Review of the Literature and Analysis of Results in Two Hundred Sixty-Two Cases of Ocular and Adnexal Pathology

IRWIN S. TERNER, M.D., M.Sc.
IRVING H. LEOPOLD, M.D., D.Sc., Philadelphia
and
ISADORE J. EISENBERG, M.D., Harrisburg, Pa.

During the past two decades there has evolved a new phase of exploration in medical science dealing with the application of artificial radioactive isotopes in medical research. Recent studies by Thomas and associates,* Town,† Dunphy and associates,‡ Eisenberg and associates,§ and Kennedy and associates [9] indicate the usefulness of radioactive phosphorus in the diagnosis of intraocular neoplasms. The present study was undertaken in order to gain more experience in the use of P^{32} in a variety of ocular pathologic conditions and to enlarge upon the original series of cases in this laboratory, to develop a method which would differentiate between inflammation and neoplasm, and to apply this technique, if possible, to the ocular adnexa.

Received for publication Sept. 26, 1955.

From the Research Department, Wills Eye Hospital.

Performed under Atomic Energy Commission Authority 17818.

Thesis submitted by Dr. Terner to the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science for graduate work in Ophthalmology.

* References 1 and 2.

† References 3 and 4.

‡ References 5 and 6.

§ References 7 and 8.

Artificial radioactivity was discovered by Curie and Joliot [10] in 1934, but it was not until 1936, when Lawrence ‖ and his associates developed the cyclotron, that the supply of artificially produced radioisotopes became sufficiently abundant to allow widespread research. Since the advent of the nuclear reactor, artificial isotopes have become so plentiful that there are 175 clinics and research laboratories in the United States at the present time using isotopes thus produced in diagnosis, therapy, and laboratory investigations. Also, there are over 150 institutions in 27 countries outside the United States to which isotopes have been made available.[14]

There are four major approaches to the application of radioisotopes in medicine. First, the assimilation, distribution, and excretion of a radioisotope may be followed quantitatively by direct measurement of samples of tissues after their removal from the body. Second, measurement of accumulation of radioisotopes may be observed directly in organs and tissues in vivo by measurement of radioactivity in situ in these structures. Third, radioautography may be employed. Finally, radioisotopes may be used therapeutically.

Hamilton,[15] in discussing the use of radioactive tracers states:

> The fundamental postulate upon which rests the value of the artificial radioelements as tracers is the fact that the radioactive isotope of a stable element differs only in its property of radioactivity; the chemical and physiological properties of the two forms of the element are identical so long as

‖ References 11 to 13.

the radiations from the radioactive isotope are not sufficiently intense to produce physiological changes. This limiting factor is not of consequence in tracer studies, since the amounts of radioactive material needed for this type of investigation are far too minute to produce any chemical or physiological changes by the action of their radiation.

HISTORY OF APPLICATION OF RADIOACTIVE PHOSPHORUS IN MEDICINE

In 1923 Hevesy [16] designed the first isotope experiment observing the uptake of a naturally occurring isotope, radioactive lead, by plants of the horsebean. He immersed the plant roots from 1 to 48 hours in a solution containing a mixture of lead nitrate and thorium B and noted that the assimilated lead was not combined with carbon within the plant, but that it existed in the form of a dissociable salt, which was soluble. Since lead is not normally metabolized by plants, the use of a naturally occurring isotope as a tracer was of limited value.

The first to employ artificial radioactivity in medical research were Chiewitz and Hevesy.[17] They investigated phosphorus metabolism in rats with the aid of P^{32}. They confirmed the theory that bone is a dynamic rather than a static structure by their observation that in the adult rat 30% of the phosphorus atoms deposited in the skeleton was removed in the course of 20 days. The average time which a phosphorus atom spends in the organism of a normally fed rat, they stated, is two months.

Radioactive phosphorus was the first isotope to be employed in the treatment of disease. Lawrence, in association with Tuttle, Scott, and Connor,¶ pioneered much of the early investigative work on the therapeutic possibilities of radioactive isotopes. The fact that when radioactive phosphorus was fed to normal animals a large percentage was deposited in bone suggested to these workers the possibility of using P^{32} as a source of therapeutic radiation in leukemia.

In experimenting with the phosphorus metabolism of normal and lymphomatous animals, they found that the phosphorus exchange differs little in the whole animal but that individual tissues show a marked difference. Thus, there exists a competition between malignant and normal tissue for phosphorus. However, the total phosphorus content of a tissue does not necessarily determine the uptake or exchange of a given dose of phosphorus in that tissue. The latter was determined by the rate of metabolism of the element in question in a particular tissue, and this could be complicated by the growth of new tissue.

In a series of studies on the phosphorus metabolism of normal and leukemic mice, these same investigators # found that the uptake or exchange of P^{32} is associated with the metabolism of the many inorganic and organic compounds (nucleoproteins, phospholipids, etc.) and with the building of new tissue, which contains phosphorus as an essential constituent. In the case of leukemic tissue the greater uptake and exchange seems to be related to, first, the rapid growth of new tissue and, second, the greater rate of metabolism of this tissue. It was also demonstrated that leukemic infiltration is accompanied by an increase of several fold in the uptake and retention of P^{32} by the nucleoprotein and acid-soluble fractions of mouse liver, spleen, and lymph nodes. The whole body retention of phosphorus given to leukemic mice was found to be higher than that of normal mice.

Erf and Lawrence * studied the uptake of radioactive phosphorus in normal subjects and in patients with leukemia, polycythemia rubra vera, and neoplastic tissue, such as neuroblastoma, seminoma, melanoma, and fibrosarcoma. They observed marked clinical and hematological evidence of improvement in patients with polycythemia rubra vera after treatment with P^{32}. There was a noticeable increase in concentration of P^{32} in the circulating white blood cells after intravenous administration as compared with oral ingestion. They also found that malignant tissues

¶ References 18 and 19.

References 20 to 24.

* References 25 to 31.

or tissues infiltrated with malignant cells retain much more P^{32} than normal tissues.

Many investigators have studied the rate of turnover of P^{32} by normal and neoplastic tissue. In a group of unique experiments, Marshak † showed that nuclei of tumor tissue accumulate more P^{32} than do normal liver nuclei. This, he claimed, is due to their mitotic activity rather than a form of metabolism peculiar to tumor cells. From the rate of P^{32} uptake by nuclei, he calculated that a new lymphoma nucleus is synthesized on the average of once every 27 hours. He stated that this is in agreement with the observed rate of growth of the tumor.

Jones, Chaikoff, and Lawrence ‡ determined the rate of phospholipid turnover in four types of transplantable mice tumors (mammary carcinoma, lymphoma, lymphosarcoma, and sarcoma 180). They found that cell type does not determine the level of phospholipid activity in a tumor. However, each tumor was found to maintain a characteristic phospholipid turnover whether grown singly or grown in the presence of two or three distinctly different types of tumors in the same animal. They concluded that the phospholipid turnover of a tumor is not determined by the metabolism of the host, although it may be modified by the host.

In another group of well-controlled experiments, these same investigators [36] studied first the phosphorus metabolism of the soft tissues of normal mice at various intervals up to 73 hours after injection of P^{32}. With the exception of brain, all tissues showed a characteristic response to P^{32} administration. There was a sharp rise in the concentration of P^{32} early, with a maximum deposition between 5 and 10 hours, followed by a slow leveling of the curve, as compared with the initial peak. Brain tissue showed a progressive increase in the amount of P^{32} deposited long after the other tissues had attained their maximum concentration. However, the activity in brain tissue was lower than in any other tissue. The highest activity of normal tissues on the basis of turnover was found to occur in liver, small intestine, and kidney.

With the phosphorus metabolism of the soft tissues of the normal animals established, they proceeded to study the rate of uptake of P^{32} by neoplastic tissues as compared with the normal tissues of the host.[37] Mice of the A strain were used, and tumors were produced by inoculating particles by the trocar method. Their procedure included the following combinations of fraternal tumors: (*a*) mammary carcinoma and lymphosarcoma; (*b*) lymphoma and lymphosarcoma; (*c*) lymphoma, lymphosarcoma and mammary carcinoma. Two groups of each of the above combinations were utilized. At the time the samples were taken, the first group of tumors were early in their development, while the second group were late in their development. Figure 1 reveals all of their essential data of the tumor study combined with figures for the normal tissues. It is seen that neoplastic tissues show a high and rapid uptake of P^{32} early after the administration of the isotope. The level of their phosphorus activities resembles the most active of the normal tissues, namely, liver, kidney, and small intestine. However, once the neoplastic tissues take up P^{32}, they show a pronounced capacity for retaining it over long periods of time in comparison with normal tissues. As will be seen shortly, the findings in the present clinical investigation corroborate the in vivo observations made by Jones, Chaikoff, and Lawrence,§ and this phenomenon can be applied for use as a test in differentiating intraocular malignancy from inflammatory lesions of the eye.

More recently, Schulman, Falkenheim, and Gray [38] found that the rate of phosphorus turnover by gastric carcinoma is at least 45% higher than that by noncancerous gastric mucosa. They also observed that the increased rate of phosphorus turnover determined by P^{32} uptake is limited to the carcinoma itself and is not evident in the adjacent normal tissue.

† References 32 and 33.

‡ References 34 and 35.

§ References 34 to 37.

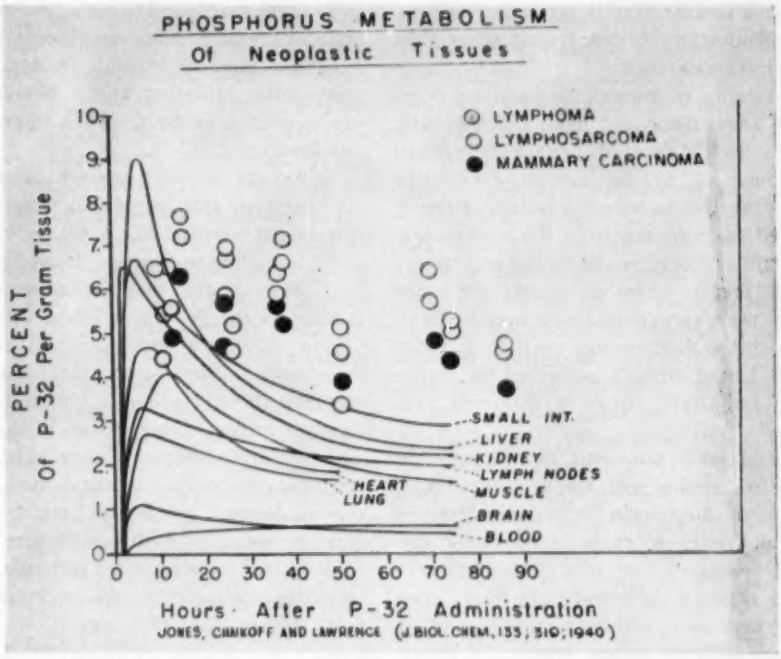


Fig. 1.—Jones, Chaikoff, and Lawrence studied the phosphorus metabolism of the soft tissues of normal animals, as well as malignant tissues transplanted into these same animals with P^{32}. They proved that once neoplastic tissues take up P^{32} they show a pronounced capacity for retaining it over long periods of time in comparison with normal tissues.

APPLICATION OF RADIOSOTOPES IN TUMOR DETECTION

In 1942 Marinelli and Goldschmidt [39] studied the deposition of P^{32} in the superficial tissues of three patients undergoing treatment with this isotope. In all three cases—one of melanoma, the other two of mycosis fungoides—both P^{32} pick-up and rate of elimination in the affected areas were found to differ radically from those of normal skin. In mycosis fungoides all of the lesions tested in each patient showed the same increased activity throughout the period of investigation. However, in the case of melanoma it was found that in the course of time the activity of the melanotic nodules increased with respect to that of normal skin. This apparently is due to a capacity for melanoma to retain P^{32} over a prolonged period of time as compared with normal tissues, including skin, rather than an ever-increasing concentration of P^{32} in melanoma per se, as one might be led to believe.

Low-Beer and his associates || studied the uptake of P^{32} by lesions of the breast in 80 patients. They injected 300μc to 500μc of P^{32} intravenously and detected radioactivity with a thin, end-window Geiger-Müller tube. Several series of measurements were made within 48 hours after injection. In 16 out of 17 benign breast lesions there was no detectable increased uptake as compared with a similar area of the opposite, normal breast. In 41 patients with malignant breast lesions, all exceeded by more than 25% measurements taken over comparable apparently normal tissues. In four patients with benign inflammatory lesions there was a marked increase in P^{32} uptake. Since the diagnosis of inflammation was obvious in three out of four of these cases, no attempt

|| References 40 to 42.

was made to differentiate between neoplastic and inflammatory breast lesions other than on clinical appearance.

The ability of tumors to fluoresce when viewed under ultraviolet light, and also their capacity for uptake of certain fluorescent dyes, has led to the use of radioactive fluorescent dyes in tumor detection. Herly [43] reported that differences in the macroscopic appearance of benign and malignant tumors of the breast were enhanced when the tumors were viewed under ultraviolet light. When this technique was used in a series of 200 breast tumors suspected of malignancy, only one error in diagnosis was acknowledged.

The fact that neoplastic tissues have the ability to combine with the acid chromogen dye sodium fluorescein ¶ prompted Moore # to employ it in 46 cases of neoplastic disease. He injected 5 cc. of a 20% solution of the dye between three and eight hours prior to surgery. Best results were obtained in 12 cases of brain tumor, where the lesions were verified by aspiration needle biopsy if they were subcortical. In the 46 cases observed there were 9 failures, the majority of which occurred in large, bulky abdominal tumors. He observed that necrotic tumor tissue did not fluoresce.

In an effort to extend the clinical value of the fluorescein test, radioactive derivatives of the dye were prepared to contain I^{131}.* Since radioactive iodine is mainly a gamma emitter, concentration and, therefore, localization could be obtained externally prior to surgery in suspected cases of central nervous system tumor. Preliminary experiments by Moore, utilizing induced brain tumors in mice, revealed the concentration of dye in the tumor tissue to be as high as 80 times that found in the adjacent normal brain. Clinically, however, Moore's results were not accurate enough to employ this preoperative procedure as the sole diagnostic test of central nervous system tumor localization.

Ashkenazy and his group † studied over 200 patients with central nervous system tumors and reported 95.5% accuracy in diagnosis, using the radioactive diiodofluorescein test. They stated that the affinity of the radioactive dye for tumor tissue was related to the cellularity and vascular pattern of the tumor. They noted that after deep roentgen therapy a higher concentration of the radioactive dye was found in the tumor.

Selverstove, Solomon, Sweet, and Robinson ‡ obtained precise localization of cerebral tumors beneath or on the surface of the brain at operation with a miniature Geiger-Müller tube the size of a ventricular needle employed as a probe. These investigators first studied the P^{32} uptake in cerebral tumors as compared with normal gray and white matter. They found that the radioactivity of tumor tissue ranged from 5.8 to 110 times greater than that of adjacent normal white matter. The activity of gray matter was ordinarily somewhat greater (about one to two times) than that of white matter, but never approached that of tumor tissue. The concentration in tumor appeared to increase with increasing cellularity in tumors of the same group. They also found that the maximum concentration ratios were usually reached on the second or third day after injection. In a series of six cases of glioblastoma multiforme they noted that the relative activity of the tumor showed an increase and a subsequent fall with increasing time intervals from injection of P^{32} to the taking of samples. This suggested that there may be an optimum time at which the activity ratio is at a maximum. The dosage of P^{32} administered and the time interval after injection when readings were determined varied considerably in their study.

¶ Basic dyes (positively charged) are readily able to penetrate into the central nervous system, while acidic dyes (negatively charged) are not. However, under certain pathologic conditions (brain tumor, brain abscess, etc.) the blood-brain barrier is destroyed and an acidic dye rapidly penetrates into the area of the lesion, but not into the surrounding normal brain tissue.

References 44 and 45.

* References 46 to 52.

† References 53 and 54.

‡ References 55 to 57.

P^{32} has been employed in the detection of testicular tumors by Roswit, Sorrentino, and Yalow.[58] After an oral dose of 300μc to 500μc of P^{32}, readings with an end-window Geiger-Müller tube were taken at 2, 4, and 24 hours. The counts were found to be maximum in 24 hours. They compared the activity of the suspected testicular tumor with a comparable area over the other, normal testicle and considered a differential uptake of up to 25% as the upper limit for normal testicle, as well as benign lesions. A difference of greater than 25% was regarded as suggestive of malignancy. In a total of six cases (a preliminary report) which came to surgery and histologic study, four diagnostic tests were correct, while there was one false-positive test and one false-negative test. The false-positive test occurred in a case of nonspecific granuloma which showed a differential uptake of greater than 50%. The false-negative test, they explain, was due to a thick layer of normal tissue surrounding a malignant testicular tumor, thus preventing the short, penetrating beta rays from reaching the Geiger-Müller tube.

DIAGNOSTIC USE OF RADIOISOTOPES IN OPHTHALMOLOGY

With the successful use of radioactive isotopes as an aid in the diagnosis of tumors in other fields, their application in the field of ophthalmology, where correct diagnosis and interpretation of intraocular lesions are paramount in the prevention of unnecessary enucleation, became inevitable.

Thomas, Krohmer, and Storaasli,[1] at the Western Reserve University School of Medicine, applied the measurement of P^{32} uptake to the diagnosis of intraocular tumors in eight cases in which the etiology of retinal elevation was in doubt. They used a small, thin, end-window, halogen-quenched counter tube for measurements in the anterior half of the eyeball. After a dose of 500μc of P^{32} was given intravenously, readings were taken one-half hour, one hour, and one and one-half hours later. They compared readings over the lesion in the pathologic eye with similar areas on the normal eye. Of the six eyes in which the counts were significantly higher over the area of the suspected tumor, five were enucleated and proved to contain malignant melanomas. The other lesion was diagnosed as metastasis from carcinoma of the breast and enucleation was withheld. One of their eight cases was of inflammatory origin, and the eye showed an increased uptake over the lesion, as well as in the other four quadrants. They concluded, therefore, that tumor was unlikely in that case. In all their cases the lesions were in the anterior portion of the choroid and easily accessible for the counting procedures. In a later report,[2] Thomas and co-workers modified their technique so that all counts were made in the same eye; that is, counts over the tumor site were compared with counts over an unaffected portion of the same eye. They state that a selective uptake ratio of 1.4 or higher is very strongly suggestive of tumor. This is comparable to 40% or more "greater than normal" in the method advocated by Eisenberg and associates.[7]

Town[3] reported on 20 cases of retinal detachment in which P^{32} uptake was used as a diagnostic procedure in order to differentiate between serous and solid lesions. In this series three cases were considered positive. He believes this test to be so valuable that it is performed routinely in all retinal detachment cases on his service at the Jefferson Medical College Hospital.

Dunphy and Selverstone[5] studied the uptake of radioactive phosphorus by normal and neoplastic ocular tissues in vitro. Intravenous injection of P^{32} was given prior to surgery. Following enucleation, weighted aliquots (50 to 75 mg.) were taken from each sample, dried, and assayed by means of an end-window, Geiger-Müller counter. Owing to the avascularity of the cornea, they used its uptake as a base line and created an "activity ratio" of tissue by means of the formula

$$\frac{\text{counts/min/mg. in tissue}}{\text{counts/min/mg. in cornea}}$$

These investigators observed that P^{32} concentrated in the vascular tissues of the eye more than in the avascular tissues and intra-

ocular fluids. They demonstrated that the activity of the tumor was higher than the activities of choroid and retina, but normal retina and choroid from an eye containing a malignant neoplasm could show abnormally high counts. They concluded, therefore, that the presence of an increased count over one portion of an eye containing a tumor could indicate the presence of a neoplasm, but not necessarily its exact location.

In a more recent paper, Dunphy, Dreisler, Cadigan, and Sweet [6] reported on 12 eyes which were studied intact following enucleation. One dose of 20μc of P^{32} per kilogram of body weight for adults and 8μc of P^{32} per kilogram of body weight for children was administered intravenously at various time intervals prior to enucleation. Of the eight eyes with malignant tumors, all but one showed a greater uptake of P^{32} over the tumor site than over the anterior half of the globe. The remaining case was a malignant melanoma of the iris. An in vivo count was attempted with the Robinson-Selverstone brain probe. Since this instrument is approximately the size of a ventricular needle, with a diameter of 2 mm., and the sensitive area of the probe is tubular, and not limited to the portion in contact with the tissue overlying the lesion, no increased counts were found over the lesion as compared with the anterior half of the globe. The authors state that the failure in this case is due to the unsuitability of this type of probe for in vivo work on the eye. Following enucleation this same eyeball yielded local differences in counts, so that localization of the tumor could be made on that basis.

Trevor-Roper, Newton, and Nicholson [59] attempted to use radioactive diiodofluorescein in the diagnosis of intraocular tumors. They found no significant difference in uptake over the eye containing malignant melanoma as compared with the normal eye.

Leopold, Eisenberg, and Hallett § also used radioactive diiodofluorescein in three cases of intraocular neoplasm. No increased uptake of the radioactive dye could be ascertained over the tumor areas as compared with readings from the normal eye. They explain the failure of this isotope in ocular tumors by the fact that radiation from normal tissues surrounding a malignant ocular lesion masks the increased radiation from the lesion itself, owing to the penetrability of gamma rays (Fig. 2).

Eisenberg, Leopold, and Sklaroff [7] employed a method whereby a norm from the nonpathologic eye was obtained by taking counts with a small, end-window halogen-quenched counter tube at the limbus at 3, 6, 9, and 12 o'clock 30 to 60 minutes after 500μc of P^{32} had been injected intravenously. These readings were of one minute's duration, and an average of these counts was then obtained. Next, the counter was placed as close as possible to the lesion on the pathologic eye. Repeated readings of one minute's duration were made. The formula $\frac{H-X}{X} \times 100 =$ "percentage greater or less than normal" was used, where H equals the average highest count in the pathologic eye and X equals the average count of the normal eye. In 45 normal eyes the "percentage greater than normal" was never more than 28. These investigators therefore arbitrarily set their criteria for positivity at 30% or more above normal for readings taken up to one hour after injection. They concluded that neoplasms in the anterior portion of the globe showed a significant detectable concentration of P^{32} one hour after injection, while those in the posterior portion varied in their detection of concentration. Also, active inflammatory lesions showed concentrations of P^{32} above 30%, while serous retinal detachments showed no detectable uptake of P^{32} unless they were of inflammatory etiology. Thus, the problem of obtaining false-positive tests in inflammatory lesions threatened to eliminate this test as a diagnostic procedure in certain cases of intraocular pathology.

Bettman and Fellows [60] have described the many variables encountered when studying P^{32} uptake in ocular tissues. These in-

§ Leopold, I. H.; Eisenberg, I. J., and Hallett, J. W.: Unpublished data.

clude the easily controlled variables, such as dose of P^{32} administered and the length of time between injection and the time readings are taken. Other variables, they state, depend on the fact that the eyeball acts as a hollow sphere, with only a narrow rim of vascular tissue—the uveal tract—taking up detectable amounts of P^{32}. They found that angulation of the tube is important in that greater counts are obtained when the tube is pointed backward toward the macula rather than held tangential to the globe.

normal" 24 hours after injection as compared with the one-hour calculation. They have therefore modified their criteria for positivity to include readings at 1 hour and 24 hours after injection.

Kennedy, Glasser, and Kazdan [9] reported on the use of the P^{32}-uptake test in 24 cases of intraocular pathology. In 11 non-neoplastic lesions there was no significant uptake of P^{32} over the lesion in the pathologic eye. However, a significant increased uptake was observed in nine cases of malignant neo-

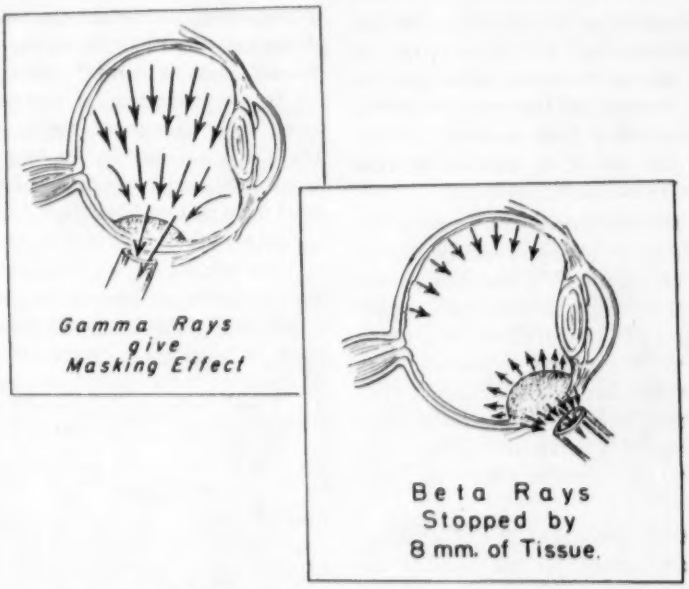


Fig. 2.—Schematic illustration of the masking effect of gamma rays.

Also, the vascularity of the extraocular muscles and tumors plays an important factor in the counting rate. They suggest that the value of P^{32} as a diagnostic agent in tumor detection could be enhanced if counts were made at much longer intervals after injection of the isotope.

More recently, Eisenberg, Terner, and Leopold [8] have demonstrated an increased accuracy of the P^{32} uptake test in cases of intraocular pathology by including readings at specific time intervals after injection. They found that in most cases of neoplasm there is a rise in "percentage greater than

plasm, while there was no significant increased uptake in three cases of melanosarcoma. The authors attribute the posterior location of the lesions as the cause of failure in these three cases. They also observed that there was an increased uptake ratio in several cases of malignant melanoma 24 hours following injection. This corroborates the observations of Eisenberg, Terner, and Leopold.[8]

The only paper in the literature to date completely discrediting the P^{32}-uptake test as employed in ophthalmology has been published by Snodgrass, Lenihan, and Prim-

rose,[61] of Great Britain. They report a series of four cases of ocular malignant melanoma in which a dose of between 180μc and 220μc of P^{32} was given intravenously one to two hours before readings were taken. They claim that no significant difference in uptake was found between diseased and healthy eyes. However, the dose employed was less than one-half the amount currently used in this country for a successful test.

POSSIBLE THERAPEUTIC APPLICATION OF RADIOACTIVE ISOTOPES

The application of radioisotopes in the field of ophthalmology has been limited at the present time to detection rather than to therapy of intraocular tumors. However, many attempts have been made in regions other than the eye or its adnexa to treat neoplasms with radioactive isotopes.

Four specific approaches to therapy which may show promise, with possible application in ocular tumors, are (1) metabolic placement of a systemically administered radioactive isotope; (2) combined use of x-radiation followed by metabolic placement of a systemically administered radioactive isotope; (3) local injection or topical application of a nonsoluble radioactive isotope, and (4) use of slow-neutron-capturing substances.

The metabolic placement of P^{32} in cancer has been investigated for its possible use as a therapeutic agent by many workers. Kenny and his associates[62] found that P^{32} was preferentially absorbed by osteogenic sarcoma and lymphosarcoma tissue to a greater extent than by carcinoma of the breast. They suggested the use of P^{32} therapeutically in these lesions.

Reinhard, Moore, Bierbaum, and Moore,[63] in a comprehensive review of the literature and report on the treatment of 155 patients with various blood dyscrasias, lymphomas, and other malignant neoplastic diseases, stated that there was no reason to believe that P^{32} was a satisfactory therapeutic agent for the treatment of lymphoepithelioma, malignant melanoma, carcinoma of the gall bladder, carcinoma of the breast, Ewing's tumor, mycosis fungoides, and xanthomatosis.

Forrsberg[64] found that breast cancer metastasis to bone absorbed greater amounts of P^{32} than other tissues. He suggested possible therapy with P^{32} in such cases. Later, in studies on the Brown-Pearce rabbit carcinoma, Forrsberg and Jacobsson[65] observed that the concentration of P^{32} in metastasis compared with that in organs with a high metabolic rate, such as liver, kidney, and spleen, was about unity. Therefore, this isotope was valueless in destroying or preventing the development of metastasis of this tumor without damaging vital organs. Friedell and Storaasli[66] attempted to use P^{32} in the treatment of carcinoma of the breast with widespread metastasis to bone. There was no increase in longevity established, although they did obtain definite relief from pain in 10 of their 12 cases.

Hertz[67] used testosterone and estrogens as pretreatment in an attempt to increase the P^{32} uptake of tumors. In hopeless cases of advanced metastatic carcinoma of various types he obtained a concentration of 15 to 20 times in tumor tissue, as compared with 2 to 3 times in normal (control) tissues.

The possible use of P^{32} as a therapeutic agent in certain brain tumors was suggested by Erickson, Larson, and Gordon.[68] By fraction studies, they found that the highest concentration of P^{32} was in the acid-soluble fraction early, but their data suggested a progressive accumulation of P^{32} in the nucleoproteins later.

In reviewing the use of P^{32} in localization of brain tumors, Sweet[69] states that, since active tissue, such as liver and bone marrow, take up as much P^{32} as brain tumors, this substance cannot be used as a therapeutic agent. The reason that the substance is valuable in tumor localization, he states, is that the normal brain takes up so little, rather than that the tumor takes up an extraordinary amount.

Brucer,[70] in discussing research with radioisotopes, states:

> Even though it has been a continuous disappointment, the metabolic placement of radiation is still

the greatest challenge in the field of therapeutic radioisotope research.

The combined effect of x-radiation followed by the metabolic placement of a systemically administered radioactive isotope has been previously discussed; Ashkenazy and his group ‖ noted that after deep roentgen therapy in brain tumors a higher concentration of the radioactive dye was found in the tumor than in normal tissue. Marinelli and Kenney [71] studied the difference in uptake of P^{32} in irradiated and nonirradiated mice and found a greater P^{32} content in the bone of the irradiated leg than in either the bone of the nonirradiated leg of the same animal or in that of the control.

Working with lymphoma cells, Marshak ¶ found that irradiation with 200 r altered the distribution of P^{32} in the lymphoma cell, markedly increasing the concentration in the nucleus shortly after irradiation, while the concentration of P^{32} in the cytoplasm decreased with time after irradiation. He suggested that the altered distribution was correlated with the inhibition of mitosis.

These three studies suggest the possibility of approaching therapeutic concentration levels in tumors with initial employment of x-radiation, followed by administration of a radioisotope which would concentrate in tumor tissue, such as P^{32}. According to Aebersold,[14] if the concentration could be elevated to 100 times that of normal tissue, P^{32} would then exert a therapeutic effect in malignant tissue.

The effect of insoluble radioactive phosphorus (chromium phosphate) was studied by Allen, Hemplemann, and Wornach.[72] They injected radiophosphorus as an insoluble salt (chromium phosphate) around the periphery of transplanted spontaneous mammary adenocarcinoma in the C-57 strain of mice, with resulting regression of the tumor. They found that where the neoplasms were larger than one-fifth the body weight of the animal, a fatal toxemia often resulted from absorption of the broken-down tumor tissue.

Low-Beer [73] used radioactive phosphorus as an external therapeutic agent in the treatment of basal-cell carcinoma, warts, and hemangioma. His results indicated that P^{32} could be used in these conditions but that other, well-established, therapeutic procedures were considered more satisfactory.

The use of slow-neutron-capturing substances has received attention as a possible therapeutic measure since Kruger [74] first applied a basic principle of physics in experimenting with tumor fragments. It is known that fast neutrons are effective in destroying tissue, while slow neutrons per se are relatively harmless when directed into tissue. When, however, slow neutrons are directed into the element of boron, the nucleus of boron captures a slow neutron and then explodes, emitting two heavy ionizing particles in opposite directions—an alpha particle and a lithium nucleus, both of which produce dense ionization and, therefore, are effective in destroying tissue. Kruger bathed tumor fragments in a nontoxic solution of boric acid and then irradiated them with slow neutrons. He then injected these same fragments into mice and noticed a marked decrease in the number of "takes" as compared with the controls. He concluded that the boron disintegration products were responsible for the death of the tumor cells and that these in vitro experiments indicated that neoplastic cells could be destroyed in vivo if sufficient boron could be applied to the tumor.

Zahl, Cooper, and Dunning [75] injected transplantable mouse sarcomas in vivo with various forms of slow-neutron-capturing materials, such as boron. When the whole animal whose tumor was so injected was irradiated with slow neutrons, a significant degree of tumor regression was observed. They stated that this tumor regression is attributed to the localized ionization resulting from the nuclear disintegration products of the capture process. They considered that for any possible future employment of the

‖ References 53 and 54.

¶ References 32 and 33.

TABLE 1.—*Summary of 262 Cases*

Lesion	Total	Positive	Negative	Surgical or Pathologic Confirmation
1. Intraocular malignancies				
A. Malignant melanoma	30	27	3	30
B. Retinoblastoma	6	1	5	6
C. Metastatic carcinoma	1	1	0	0
2. Inflammatory retinal detachment	28	1	27	5
3. Serous retinal detachment	67	0	67	64
4. Choroidal detachment	3	0	3	0
5. Inflammatory lesions without detachment	15	1	14	2
6. Iris lesions				
A. Benign melanoma	9	0	9	0
B. Malignant melanoma	1	1	0	0
C. Cyst	2	0	2	0
D. Leiomyoma	1	0	1	1
E. Pigment granule in angle	1	0	1	0
7. Glaucoma				
A. Primary	1	0	1	0
B. Secondary	6	0	6	3
C. Absolute	15	0	15	11
8. Intraocular hemorrhage				
A. Hyphema	2	0	2	0
B. Vitreous	15	1	14	0
C. Choroidal	4	0	4	0
9. Cataracts				
A. Senile	4	0	4	2
B. Complicata	10	1	9	8
10. Phthisis bulbi	2	0	2	2
11. Miscellaneous intraocular lesions	10	0	10	0
12. Adnexal lesions				
A. Cancerous melanosis of conjunctiva	1	1	0	1
B. Pigmented nevus of conjunctiva	2	0	2	0
C. Mucocele	3	0	3	3
D. Orbital lesions				
1. Pseudotumor	2	0	2	2
2. Lymphosarcoma	1	1	0	1
3. Lacrimal gland inflammation	3	0	3	3
4. Exophthalmos	3	0	3	0
E. Lid lesions				
1. Metastatic malignant melanoma	1	1	0	0
2. Chronic granuloma	2	0	2	2
3. Pigmented nevus	1	0	1	0
4. Epitheliomata				
A. Squamous-cell	3	3	0	3
B. Basal-cell	7	6	1	7

slow-neutron-boron process in tumor therapy, some device other than simple hypodermic injection should be developed for localizing boron or lithium or related materials in malignant tissues. This, they stated, is essential in metastasis and deep-seated growths.

Sweet and Javid [76] administered boron intravenously in the form of borax to patients with brain tumors in order to determine the differential uptake of boron by brain tumors and normal brain tumors. They found that glycerin, when given concomitantly, helped to prevent the borax from entering as readily into normal brain tissue but did not affect the uptake by malignant brain tissue. In glioblastomas and metastatic carcinomas the maximum differentials in concentration were usually reached 10 to 15 minutes after injection, rarely failing to attain a 3:1 ratio. The possibility of destroying brain tumor tissue with slow-neutron therapy would seem to be likely. However, large amounts of boron were also found in muscle and bone, with variable amounts found in the skin. The destruction of these normal tissues overlying brain tumor, however, would not be a deterrent to the method, they state. Their results suggested that if the ionizing radiations in the neoplasm achieve a level four times that in the normal white matter and three times

that in the gray matter, differential destruction of neoplasm may occur.

Sweet's initial work has been followed up by Farr and his associates at the Brookhaven National Laboratory, in collaboration with Sweet.[77] They recently reported on 10 patients who were given neutron-capture therapy. All patients had proved glioblastoma. No conclusive results were obtained, but their clinical data suggest that the tumor growth was retarded to some degree by the process.

It is quite evident that therapy with radioisotopes is in its infancy. Many methods which will prove therapeutic in other regions of the body will no doubt be harmful in ocular therapy, for the delicate structures within the eye will not tolerate much radiologic abuse. However, pretreatment with hormones or x-radiation employed to enhance the concentration of metabolically placed isotopes may well find application in tracer studies. Since ocular tumors are relatively small, any increase in concentration of the isotope would help to facilitate their detection.

PRESENT STUDY

The present study encompasses 262 ophthalmologic cases which were subjected to P^{32} uptake tests (Table 1). One hundred twenty-three of these cases were published in an earlier report,[8] which has since been analyzed and revised in the light of further experience. These lesions may be divided into two groups: (1) intraocular and (2) extraocular or adnexal.

Intraocular Lesions

A total of 233 cases with intraocular lesions were tested 1 hour and 24 hours after injection, with few exceptions. Of these, there were 33 positive tests, all occurring in cases of suspected tumor. This group of intraocular lesions is further subdivided into 11 categories, and each category will be discussed individually.

A. Method.—Since, as discussed above, experimental evidence exists that tumor tissue retains P^{32} over a longer period of time than normal tissue, it was planned to include counts at varying intervals after injection of the isotope. It was theorized that cases in which malignancy was present would show a greater differential, as represented by "percentage greater than normal," in 24 hours and 48 hours. For sake of clarity, the procedure is repeated here. One hour after intravenous injection of 500μc to 750μc of P^{32},# depending on the weight of the patient, readings are taken with a small, end-window, halogen-quenched counter tube * on the normal eye at the limbus at the 3, 6, 9, and 12 o'clock positions. Counts are of one minute's duration, but several counts are taken over each area. These one-minute counts are then averaged. Next, the counter tube is placed as near as possible to the lesion in the pathologic eye. A series of one-minute counts are taken. The average count over the area of highest response is then taken. The formula $\frac{H-X}{X} \times 100$—percentage greater or less than normal is used, where H equals the average of the highest counts in the pathologic eye and X equals the average count in the normal eye. The same procedure was repeated 6, 24, and 48 hours after injection. It was soon found that complaints of irritation were common after the six-hour count, and therefore these counts were discontinued. Forty-eight-hour counts were taken until a definite trend became evident. Since they paralleled the 24-hour readings, this reading was deemed unnecessary. Also, the count in the normal eye often fell below 100 counts per minute 48

The P^{32} (radioactive phosphorus) solution was obtained from the Abbott Laboratories, Oak Ridge, Tenn. According to D. L. Tabern, the solution is prepared by the bombardment of ordinary sulfur, with the resultant formation of P^{32}, which is isolated as phosphoric acid. A few tenths of a milligram per cubic centimeter of carrier phosphate is added to minimize adsorption on the walls of glassware used in preparation. The pH is next adjusted to between 6 and 6.5 by adding a small amount of sodium acetate. The solution is then carefully treated to remove pyrogens and sediment. Following this, it is sterilized and assayed.

* Available from Anton Laboratories, Brooklyn.

hours after injection, and the statistical accuracy of the calculation was questioned.

In cases of bilateral pathology the method included readings over each pathologic area. Thus, in a case of bilateral serous detachment of the retina, readings were taken over one eye at the limbus as the normal, and then over the area of pathology in the fellow eye. This procedure was then reversed, and readings were taken at the limbus in the opposite eye and then as close as possible to the lesion in the fellow eye. In patients with one eye, readings were taken at the limbus and then as close as possible to the lesion. With the small, end-window counter tube used, background count was negligible.

In children the dose varied according to age and weight. However, 100μc was the smallest dose administered. It was found that, even though the diameter of the counter tube was 0.310 in. (8 mm.), this was rather large for the eyes of infants and small children.

As our experience increased with P^{32} testing, a general trend became evident. It was observed that when the test was performed 24 hours after injection the "percentage greater than normal" increased beyond the one-hour calculation in tumor cases, while

TABLE 2.—*P^{32} Uptake by Ocular Tumors*

Case No.	Age	Clinical Diagnosis	Pathologic Diagnosis	P^{32} Uptake, Percentage Greater Than Normal			Comment
				1 Hr.	24 Hr.	48 Hr.	
12	71	Solid retinal detachment (anterior)	Malignant melanoma	86	160	..	Large solid retinal detachment temporally
14	46	Anterior staphyloma, probably due to malignant melanoma	Malignant melanoma	82	210	..	Blind eye due to glaucoma for 5 yr.; recent tension increase
20	40	Solid retinal detachment (posterior)	Malignant melanoma	67	88	96	Large solid retinal detachment inferiorly
21	58	Solid retinal detachment (posterior)	malignant melanoma	31 31*	0 40*	.. 98*	Failure of 24-hr. count (no increase)
28	38	Solid retinal detachment (posterior)	Malignant melanoma	31	75	..	Large solid retinal detachment nasally
38	37	Solid retinal detachment (anterior)	Malignant melanoma	53	140	..	Large solid detachment superiorly
57	57	Solid retinal detachment (posterior)	Malignant melanoma	12 36* ..	66 50* 126†	79	Failure of 1-hr. count (less than 20%)
61	69	Malignant melanoma of conjunctiva	Cancerous melanosis	61	102	266	Mushroom-shaped mass attached at limbus by a pedicle; no intraocular extension; deeply pigmented conjunctiva at superior fornix
66	73	Scleral perforation of intraocular tumor; secondary glaucoma (anterior)	Malignant melanoma	55	142	170	At superior nasal portion O. D. about 8 mm. posterior to limbus; sclera appeared to be perforated by a darkly pigmented mass 2×2 mm.
70	37	Bilateral serous and unilateral (O. D.) solid retinal detachments, due to metastatic carcinoma of breast (anterior)	None	O. S. as normal 55 O. D. as normal —17	92 1	99 10	Carcinoma of breast removed 5 yr. prior to this admission; at time of test patient had metastasis to lumbar spine
94	63	Solid retinal detachment (anterior)	Malignant melanoma	57	142	141	Solid retinal detachment temporally
106	62	Solid retinal detachment (anterior)	Malignant melanoma	35 45‡	32 56‡	.. ..	Failure of 24-hr. count (no increase)
101	53	Malignant melanoma of ciliary body (anterior)	Malignant melanoma	38	55	..	Tumor protruded when keratome incision was made for cataract extraction; incision closed and enucleation performed 1 wk. later
120	68	Solid retinal detachment (anterior)	Malignant melanoma	57	87	..	Solid retinal detachment inferonasally

TABLE 2.—*P^{32} Uptake by Ocular Tumors*—Continued

Case No.	Age	Clinical Diagnosis	Pathologic Diagnosis	P^{32} Uptake, Percentage Greater Than Normal			Comment
				1 Hr.	24 Hr.	48 Hr.	
124	63	Solid retinal detachment (posterior)	Malignant melanoma	59 119*	58 179*	.. ..	Failure of 24-hr. count (no increase)
140	77	Solid retinal detachment (anterior)	Malignant melanoma	71	165	..	Large solid retinal detachment superiorly
146	34	Solid retinal detachment (anterior)	Malignant melanoma	38	86	..	Large solid retinal detachment superotemporally
147-B	36	Solid retinal detachment (anterior)	Malignant melanoma	39	48	..	Large brownish-black mass near ciliary body
148	54	Serous and solid retinal detachment (posterior)	Malignant melanoma	77	170	..	Lesion located inferotemporally
165	..	Serous and solid retinal detachment (posterior)	.....	81	99	..	Lesion located temporally
166	58	Serous retinal detachment (posterior)	Malignant melanoma	111	63	..	False-negative test
168	58	Solid retinal detachment (anterior)	Malignant melanoma	8 71§	60 87§	.. ..	Failure of 1-hr. count
170	68	Melanoma of angle with solid retinal detachment (anterior)	Malignant melanoma	99	252	..	Lesion located inferiorly
187	26	Solid retinal detachment (anterior)	Malignant melanoma	54	117	..	Lesion located superiorly
232	50	Solid retinal detachment (anterior)	Malignant melanoma	67	100	..	Lesion located nasally
238	40	Solid retinal detachment (posterior)	Malignant melanoma	89	76	..	False-negative test
240	67	Solid retinal detachment (anterior)	Malignant melanoma	93	200	..	Lesion located nasally
243	28	Solid retinal detachment (anterior)	Malignant melanoma	38	61	..	Lesion located inferotemporally
247	55	Solid retinal detachment (posterior)	Malignant melanoma	18	...	..	False-negative test
250	61	Solid retinal detachment (anterior)	Malignant melanoma	92	127	..	Lesion located temporally
254	69	Solid retinal detachment (anterior)	Malignant melanoma	39	129	..	Lesion located inferiorly
255	45	Malignant melanoma of ciliary body and iris (anterior)	Malignant melanoma	36	40	..	Lesion located inferiorly; first noticed 3 yr. ago
15	24 mo.	Retinoblastoma	Retinoblastoma	74	80	..	X-ray positive for calcification
27	6 wk.	Retinoblastoma	Retinoblastoma	72	...	..	X-ray positive for calcification
95	14 mo.	Retinoblastoma	Retinoblastoma	22	...	..	X-ray negative for calcification
163	21 mo.	Retinoblastoma	Retinoblastoma	28	12	..	X-ray positive for calcification
218	5 mo.	Retinoblastoma or pseudoglioma	Retinoblastoma	1	...	..	X-ray positive for calcification
239	9 mo.	Retinoblastoma or pseudoglioma	Retinoblastoma	5	2	..	X-ray positive for calcification

* Repeat test one week later.
† Lateral rectus muscle detached and probe placed directly over the posterior lesion.
‡ Repeat test one month later.
§ Repeat test three months later.

there was a decrease in "percentage greater than normal" in most other cases. The 48-hour readings also showed this general trend. Our criteria for positivity, therefore, were modified to include the 24-hour study. Positivity was indicated when in one hour the "percentage greater than normal" was over 30, and in 24 hours there was an increase beyond the original one-hour calculation.

One puzzling observation was the fact that in both normal and pathologic eyes an increased count was obtained over the medial portion of the sclera toward the inner canthus. When this occurred, the counter tube was placed slightly above or slightly below this area. The fact that the medial rectus muscle is inserted only 5.5 mm. behind the limbus and the tendon of this muscle measures only 3.7 mm.[78] probably indicates that the increased counts were due to the uptake of P^{32} by the muscle, rather than by the globe alone.

Fig. 3 (Case 14).—Malignant melanoma with anterior staphyloma and Reese's sign.

B. Results.—I. Intraocular Malignancies: A total of 37 patients with intraocular malignancy exclusive of iris lesions were tested (Table 2). Of these, 30 had malignant melanomas, 6 had retinoblastomas, and 1 had metastatic carcinoma from a breast lesion. All of these cases were proved pathologically except the case of metastatic malignant carcinoma, for which enucleation was withheld. Nineteen of the 30 intraocular malignant melanomas either had arisen from or extended anterior to the equator of the eye, so that they were easily accessible to the counter tube. There was only one false-negative test in this group (Case 168), and a repeat test of this case three months later revealed a positive result. There were 11 cases of intraocular malignant melanoma in which the lesion was located posterior to the equator of the eye. Of these, tests were repeated in three cases (Cases 21, 57, and 124), in which the original study revealed negative tests. Repeat tests were performed when the findings of the test were not in agreement with a positive clinical diagnosis. All of the repeat tests in the above-mentioned cases were subsequently positive. However, there were three other false-negative tests in this series of 11 posterior lesions (Cases 166, 238, and 247), which did not have repeat studies.

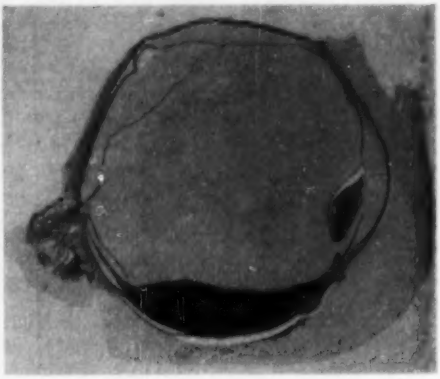
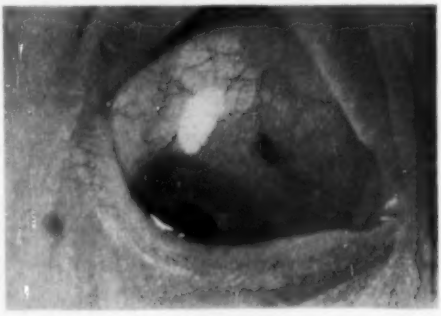


Fig. 4 (Case 14).—Anterior extension of the tumor in cross section.

Case 238 was that of a posterior lesion in which surgery for retinal detachment had

Fig. 5 (Case 66).—Scleral perforation of an intraocular malignant melanoma.



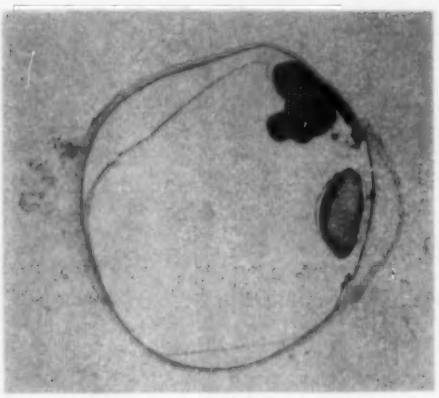


Fig. 6 (Case 66).—Anterior extension of the tumor mass in cross section.

been unsuccessful prior to the P^{32} test. The false-negative result may have been due to the fact that sufficient time had not been allowed for the postoperative inflammatory reaction to subside.

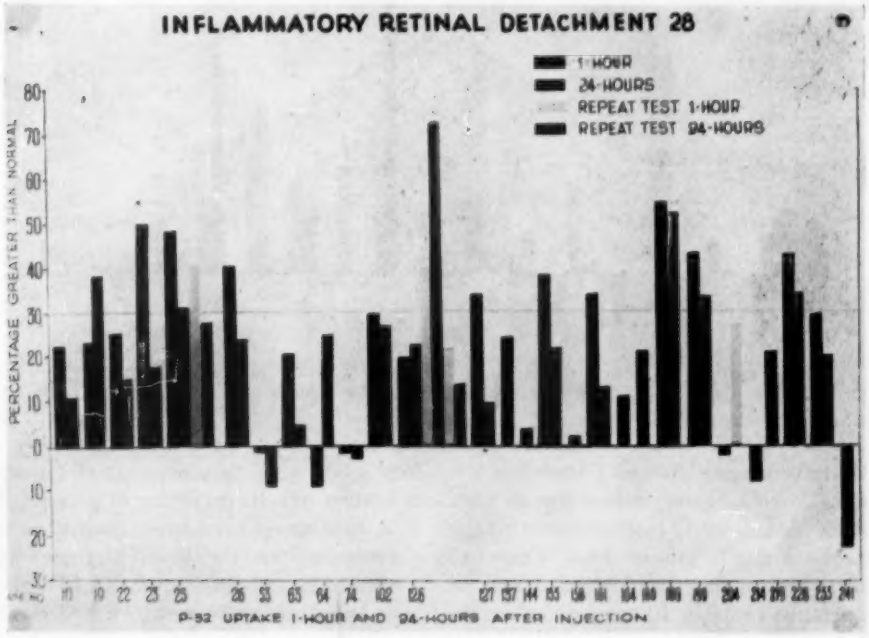
In Case 14 (Fig. 3) the lesion was diagnosed as an anterior staphyloma, probably due to malignant melanoma, which occurred in a blind eye due to glaucoma. A recent tension rise was noted. The P^{32} uptake test was positive. Figure 4 reveals the anterior extension of the tumor in cross section.

Case 66 (Fig. 5) was diagnosed clinically as a possible scleral perforation of an intraocular malignant melanoma. There was an associated secondary glaucoma. The P^{32} uptake test was positive. Figure 6 shows the anterior tumor mass in cross section.

Six cases of retinoblastoma were subjected to P^{32} testing. Only one case (Case 15) met our criteria for positivity. All but one of these cases (Case 95) had x-ray evidence of intraocular calcification. The lesion in each case extended anterior to the equator and therefore was readily accessible to the counter tube.

The one case of metastatic carcinoma had a serous retinal detachment in the left eye with a serous and solid detachment of the retina in the right eye. The left eye failed to give a positive test, while the test was positive for the right eye.

Figure 7



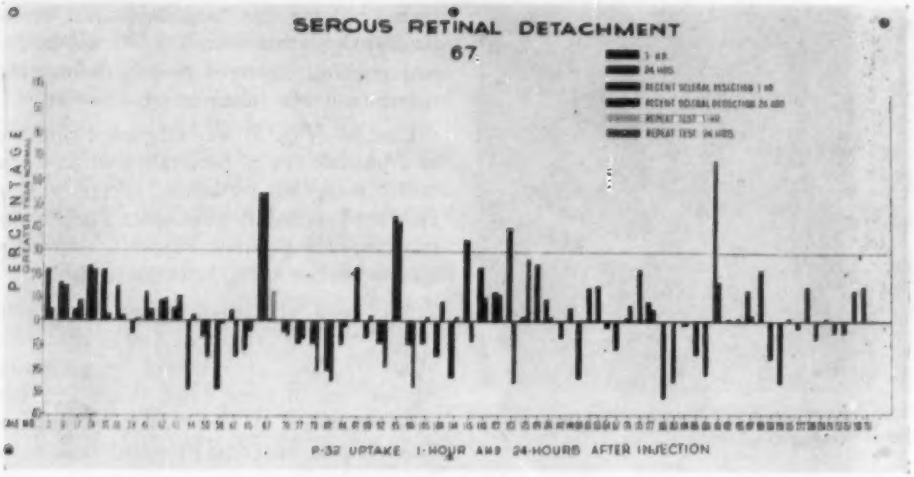


Figure 8

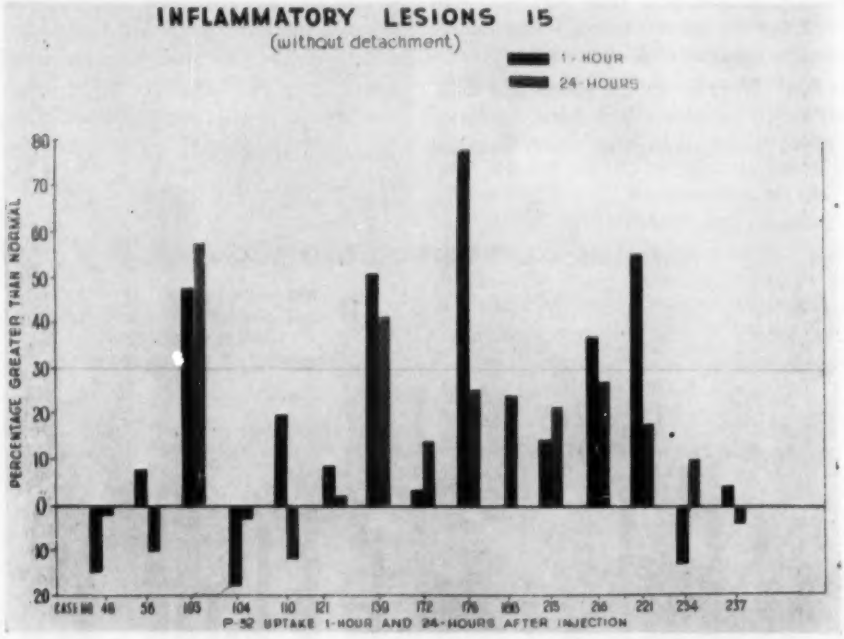


Figure 9

II. Inflammatory Retinal Detachment: A total of 28 inflammatory retinal lesions were studied, comprising 12 cases of serous retinal detachment due to inflammation, 4 cases of exudative choroiditis in children, 1 case of proliferative retinitis, 10 cases of inflammatory solid retinal detachment, and 1 case of exudative retinitis occurring in an adult. To date, enucleation has been performed in five of these cases, and the clinical diagnoses were confirmed by pathologic study. In 13 of these cases initial readings were above 30% greater

Fig. 10 (Case 103).—Nonspecific episcleritis and scleritis.

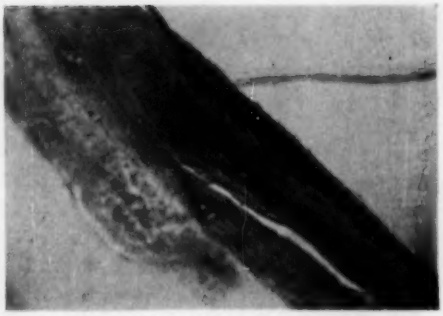


Fig. 11 (Case 103).—Microscopic section of round-cell infiltration in sclera and episclera.

than normal one hour after injection (Fig. 7). However, there was a decrease in the 24-hour calculation in all but one case (Case 126).

In Case 126 the lesion consisted of a grayish, flat, solid detachment of the retina in the superior temporal quadrant of the left eye of a 51-year-old white woman. No retinal tear was visualized. The first P^{32} uptake test was negative. Since the lesion continued to progress over a six-month period, a repeat test was performed and the result was positive. The lesion was carefully observed for several more months and appeared stationary. A third test was negative. To date, the eye has not been enucleated and the lesion is still under observation.

III. Serous Retinal Detachment: A total of 67 cases with serous retinal detachment were tested with P^{32} (Fig. 8). In no instance was there a positive test. In 64 of these cases the diagnosis has been confirmed surgically. Many tests revealed a decreased uptake of P^{32} over the area of retinal separation as compared with the normal eye. This may be attributed to the fact that less tissue is present at the site of retinal separation and therefore fewer counts per minute are obtained.

Four patients with serous retinal detachments who failed to respond to retinopexy were subjected to scleral resection. Following this, P^{32} uptake studies were performed within four months. In all four cases the one-hour uptake was over 30% greater than normal. However, in 24 hours three of the four cases showed a decrease in percentage greater than normal, while in one case (Case 67) the calculation remained as high as the

TABLE 3.—*Inflammatory Lesions Without Detachment*

Case No.	Clinical Diagnosis	P^{32} Uptake, Percentage Greater Than Normal		Comment and Location of Lesion
		1 Hr.	24 Hr.	
48	Chorioretinitis juxtapapillaris	−15	− 1	Posterior
56	Tuberculous keratitis	+ 8	−10	Anterior
103	Episcleritis and scleritis (nonspecific)	+47	+58	Anterior (false-positive test) (Figs. 10 & 11)
104	Chorioretinitis	−10	− 2	Posterior
110	Iridocyclitis	+20	−12	Anterior
121	Chorioretinitis	+ 9	+ 1	Posterior
139	Scleritis and secondary glaucoma	+51	+41	Anterior, eye enucleated
172	Uveitis, anterior	+ 3	+14	Anterior
176	Uveitis, anterior	+79	+25	Anterior
188	Inflammatory paramacular lesion	+24	....	Posterior
213	Iritis and secondary glaucoma	+14	+21	Anterior
216	Inflammatory mass near lens	+37	+27	Anterior
221	Uveitis, posterior	+65	+18	Posterior
234	Heterochromic iridocyclitis	−13	+10	Anterior
287	Macular degeneration	+ 4	− 4	Posterior

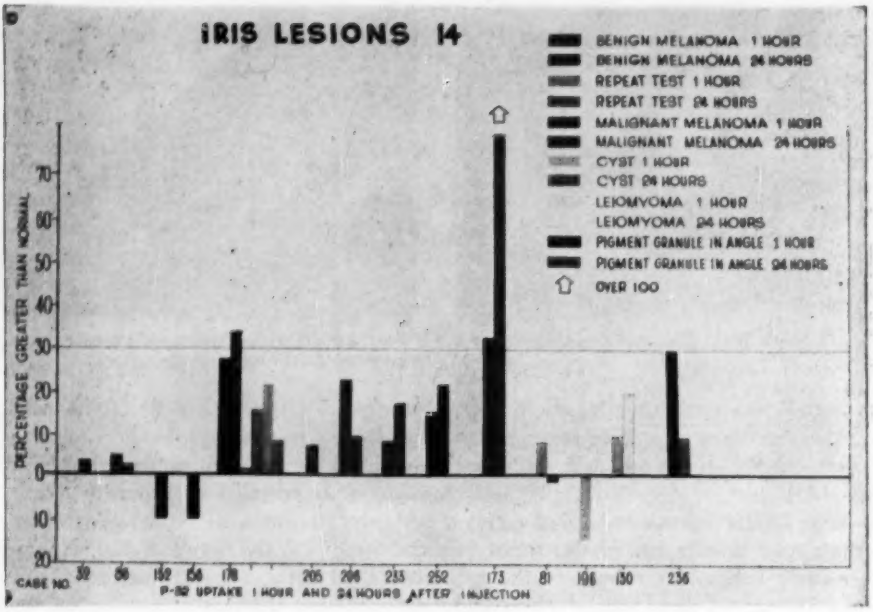


Figure 12

original one. A repeat test in this case one month later was negative. To date, there is no clinical evidence of tumor in these cases.

IV. Choroidal Detachment: Three cases of choroidal detachment were tested with P^{32}. The three tests were negative. A spontaneous remission of the detachment occurred in each case.

V. Inflammatory Lesions Without Retinal Detachment: Fifteen cases of intraocular inflammatory lesions without retinal detachment were subjected to P^{32} uptake studies (Table 3 and Fig. 9). Only two of these lesions were studied pathologically.

In this group there was one positive P^{32} test (Case 103). This occurred in an elderly white woman and involved the sclera superonasal to the limbus. The lesion was rather dark and slightly elevated, and numerous blood vessels coursed over it (Fig. 10). Clinical opinion was divided as to whether the lesion was a tumor or scleritis with a

Fig. 13 (Case 130).—Leiomyoma of iris.

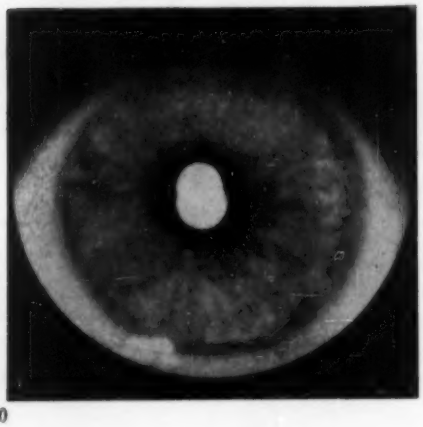
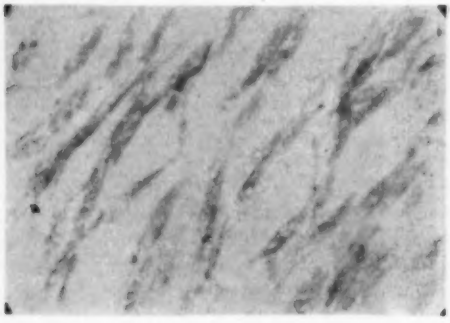


Fig. 14 (Case 130).—Microscopic section revealing myoglial fibrils; phosphotungstic-acid-hematoxylin stain.



possible staphyloma. The patient refused enucleation, but after her death the eye was made available for pathologic study. As can readily be seen in microscopic section (Fig. 11), the lesion consists of round-cell infiltration in the sclera and episcleral tissues. The test in this case, of course, was a false-positive one.

VI. Iris Lesions: There were 14 cases with iris lesions tested with P^{32} (Fig. 12). Of these, nine lesions had the clinical appearance of benign melanoma, one appeared to be a malignant melanoma, two appeared to be iris cysts, one appeared to be a leucosarcoma, and one appeared to be a pigment granule in the angle of the anterior chamber.

The only case which came to surgery was that in which the lesion appeared to be a leucosarcoma. The P^{32} study was negative. The lesion was removed surgically, and the pathologic diagnosis was reported as leiomyoma. Figure 13 shows the external appearance of the lesion, while Figure 14 reveals the myoglial fibrils with the Mallory phosphotungstic-acid-hematoxylin stain. This case has recently been reported in the literature.[81]

VII. Glaucoma: P^{32} studies were performed in 22 cases with the diagnosis of glaucoma (Fig. 15). Of these, the condition in 1 case was of the chronic simple type; in 6 cases it was secondary glaucoma, and in 15 cases, absolute glaucoma. All P^{32} tests were negative. In 3 of the 6 cases of secondary glaucoma and in 11 of the 15 cases of absolute glaucoma enucleation was performed. Pathologic examinations failed to reveal any melanomas in these eyes.

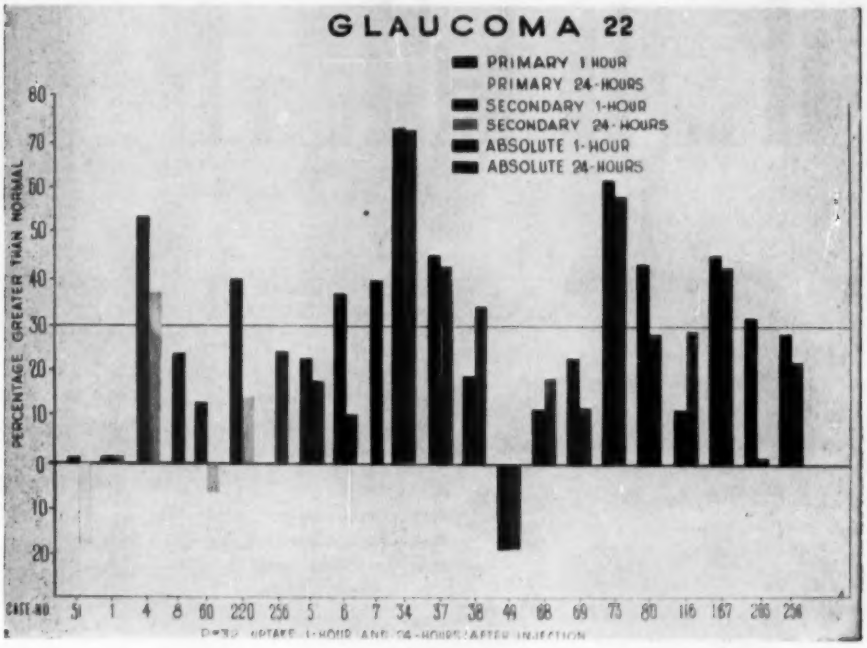


Figure 15

In one case of absolute glaucoma (Case 34) there was a marked initial rise to 73% greater than normal. In 24 hours there was no decrease or increase in uptake, making this test negative. Pathologic examination of this globe confirmed the clinical diagnosis of absolute glaucoma. No explanation can now be given for the high uptake of P^{32} in this case, though by our present criteria this test is negative.

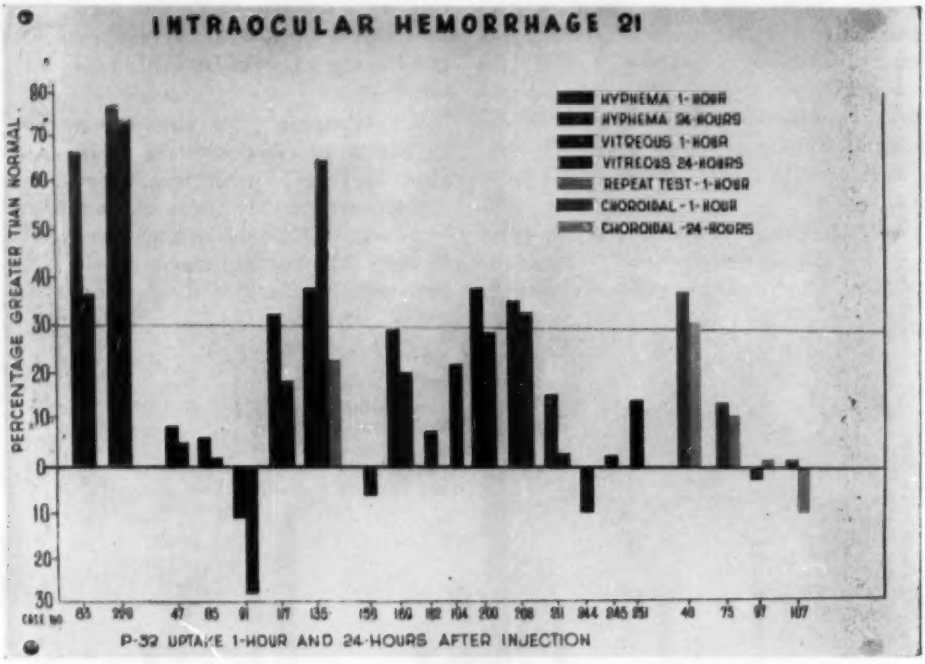
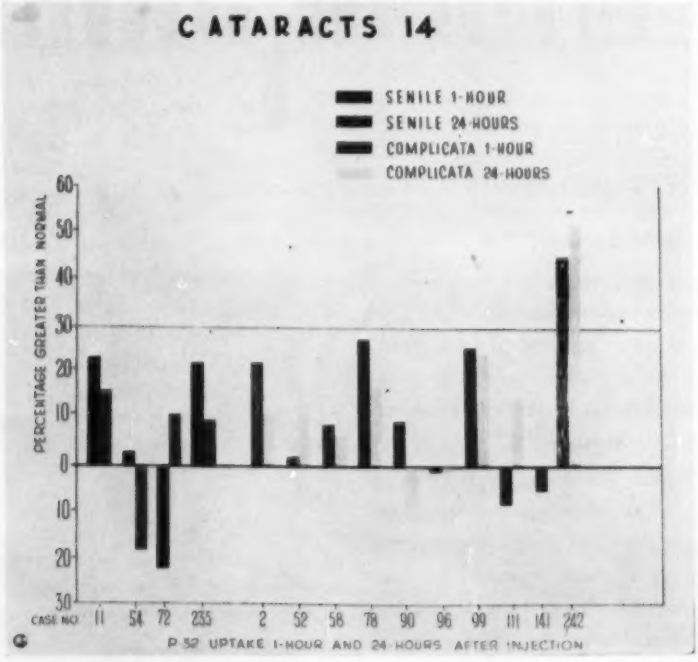


Figure 16

Figure 17



VIII. Intraocular Hemorrhage: There were 21 cases of intraocular hemorrhage in this series in which P^{32} uptake studies were performed (Fig. 16). Of these, the diagnosis was hyphema in 2 cases, vitreous hemorrhage in 15 cases, and choroidal hemorrhage in 4 cases.

All tests were negative with the exception of that performed in Case 135. The patient was referred for P^{32} study following a sudden vitreous hemorrhage in the left eye. The P^{32} test was positive. Since the fundus could not be visualized, it was decided that a repeat test should be performed a few months later, after some vitreal clearing. The test was repeated and found to be negative. To date the vitreous has not cleared entirely, and enucleation is not being contemplated at the present time.

IX. Cataracts: There were 14 eyes with cataracts subjected to study with P^{32} (Fig. 17). Of these, 4 presented senile cataract, and 10, complicated cataract. In all but one (Case 242) the P^{32} study failed to meet our criteria for positivity.

In Case 242 the diagnosis was complicated cataract due to granulomatous uveitis. There was an associated secondary glaucoma. The eye is blind and occasionally painful, but the patient refuses enucleation.

To date, five of these cases have had cataract surgery. Fundus examination failed to reveal any abnormalities in these five cases.

X. Phthisis Bulbi: Two cases of phthisis bulbi were tested with P^{32}. Both tests were negative. Pathologic study of these two eyes following enucleation revealed no intraocular malignancy.

XI. Miscellaneous Intraocular Lesions: There were 10 cases with intraocular lesions subjected to P^{32} tests which could not be classified in the above-listed categories. In the majority of these cases the lesions were diagnosed clinically as probable benign posterior melanomas, although in several cases no specific diagnosis was offered by the referring physician.

The P^{32} tests in these cases were negative. To date, none of these eyes have come to pathologic study.

C. Comment.—One of the main objectives of this study was to develop a method which would eliminate the false-positive tests obtained when only the one-hour reading was taken. Active inflammatory lesions were the commonest conditions which gave false-positive results. In the present series, there were three false-positive tests in the group of inflammatory lesions. One occurred in a case of episcleritis and scleritis, and one occurred in a case of inflammatory retinal detachment. Another occurred in a case of vitreous hemorrhage.

Three false-negative tests occurred in the series of 30 cases of intraocular malignant melanoma. The lesion in these three cases was posterior to the equator of the globe and inaccessible to the small counter tube employed.

In four other cases of malignant melanoma repeat tests were performed where the clinical diagnosis was obvious and the P^{32} uptake test had been negative. All of the repeat tests were positive. Three of these occurred in cases where the lesion was posterior to the equator of the globe, while one occurred in a lesion anterior to the equator.

There were five false-negative tests in the series of six cases of retinoblastoma, all of which extended anteriorly to the equator of the globe. There is no apparent explanation for the failure of the test in these tumors.

With the present counter tube employed, equivocal results are obtained with posterior lesions. A counter tube similar in shape to a posterior transilluminator has been developed by Thomas and his co-workers [79] and is in the process of evaluation by his group, as well as in this laboratory.

The failure of the P^{32} uptake test in cases with posterior lesions is not difficult to explain, since the distance of the tube from the lesion in these cases is greater than the maximum distance traveled by the beta rays in tissue. However, as mentioned previously, there is in vitro evidence [5] that an increased count over one portion of an eye containing a tumor could indicate the presence of a neoplasm but not necessarily its exact location. This may explain why the test is posi-

tive in some cases in which the tumor is too far posterior for the counter tube to be placed close enough to the lesion.

One postulation for failure of the test in an anterior lesion could be that an inactive phase of metabolism exists during the metamorphosis of malignant tumors. If such a phenomenon occurs, it could be assumed that the phosphorus metabolism of a malignant tumor resembles that of normal tissue at certain periods of its growth. Furthermore, if the P^{32} uptake test were performed during such a period, a false-negative result could be predicted.

It is well known that blind, painful eyes often harbor intraocular malignancies. Duke-Elder [80] states:

> A blind and painful eye so frequently contains a tumor, that on this ground alone it can be argued with a considerable amount of justification that all such eyes should be excised (Chance, 1934; Terry, 1939). A similar generalisation should be made in the case of eyes with absolute glaucoma in which the fundus cannot be seen.

In this study 11 cases of absolute glaucoma and 2 cases of phthisis bulbi had negative P^{32} uptake tests following which pathologic study revealed no intraocular malignancy.

The question frequently arises as to how soon following retinopexy and scleral resection the P^{32} uptake test could be performed with accuracy. These procedures invariably create a state of inflammation, which may give rise to erratic uptake of the isotope, with resultant unreliable counts. It has been found that once the inflammatory reaction subsides, the initial uptake is greatly increased in these cases, but usually there is a decrease in the 24-hour calculation. Therefore, it is advised that the test be performed not less than eight weeks following such surgical procedures.

The P^{32} uptake test gives less accurate results in patients with one eye, in patients with bilateral ocular pathology, in patients who have had previous ocular surgery, and in patients with posterior segment pathology.

In this study, no correlation could be made between the P^{32} uptake measured in vivo as "per cent greater than normal" and the cellular type of the malignant melanoma studied in vitro after enucleation.

The validity of the P^{32} uptake test depends upon (1) the ability of malignant tissue to concentrate P^{32}; (2) the capacity of malignant tumor tissue to retain P^{32} over a period of time, and (3) the faculty of normal tissues to excrete their initial concentration of P^{32} rapidly.

Extraocular (Adnexal) Lesions

A total of 29 cases with extraocular (adnexal) lesions were tested 1 hour and 24 hours after injection (Table 4). This group is further subdivided into three categories, which are discussed individually.

A. Method.—A dose of 0.5 mc. (500μc) of radioactive phosphorus is injected intravenously. Readings are taken with a small counter tube (the same tube that is used on the globe) 1 hour and 24 hours after injection. In the case of lid lesions, readings are taken at the outer, middle, and inner thirds of the normal lid on its external surface, as close as possible to the lid margin. These counts are then averaged. Several counts of one-minute duration are taken over each area. Next, readings or counts are taken with the end-window of the tube in direct contact with the lesion on the opposite eyelid. The same mathematical calculation as that described above for intraocular lesions is employed. A Lucite lid plate is used to shield radiations emanating from the globe and surrounding tissues. In cases other than lid lesions the method is changed so that counts over similar areas are compared. This was found necessary in lesions of the lacrimal apparatus, as well as in tumors of the orbit and sinuses.

In order to determine the maximum difference in uptake between similar normal eyelids in the same patient, P^{32} uptake was studied in 100 normal eyelids of 25 patients (Fig. 18). All of these patients were undergoing P^{32} testing for intraocular lesions. Counts were made between 90 and 120 minutes after injection. Using the average count in one lid as the normal and then taking the highest count in the opposite lid as the greatest varia-

TABLE 4.—*Extraocular (Adnexal) Lesions*

Lesion	Case No.	Age, Yr.	Clinical Diagnosis	Pathologic Diagnosis	P^{32} Uptake, Percentage Greater Than Normal: 1 Hr.	P^{32} Uptake, Percentage Greater Than Normal: 24 Hr.	Comment
Conjunctival	61	00	Cancerous melanosis	Cancerous melanosis	+ 61	+192	Deeply pigmented conjunctiva at superior fornix
	145	31	Pigmented nevus	None	+ 20	+ 9	Lesion on plica semilunaris since early childhood
	224	34	Pigmented nevus	None	+ 51	+ 24	.....
Orbital							
A. Mucocele	29	58	Mucocele, ethmoid sinus	Ossifying fibroma, ethmoid sinus	+ 20	+ 11	.....
	128	55	Mucocele, ethmoid sinus	Chronic inflammatory reaction	+ 47	+ 29	Lesion ruptured; sac wall excised
	102	32	Mucocele, frontal sinus	Not available	+ 14	— 4	.....
B. Lacrimal gland inflammation	55	19	Tumor of lacrimal gland	Sarcoid of lacrimal gland	+ 24	+ 18	No exophthalmos
	109	56	Tumor of lacrimal gland	Chronic dacryoadenitis	+100	+ 89	Unilateral exophthalmos
	136	43	Tumor of lacrimal gland	Chronic dacryoadenitis	+ 13	+ 14	Unilateral exophthalmos
C. Pseudotumor of orbit	106	76	Bilateral herniated fat masses	Pseudotumor of orbit; granuloma	Right orbit as normal + 11 Left orbit as normal — 2	+ 1 + 2	.....
	132	44	Orbital tumor	Pseudotumor of orbit; chronic granuloma	+ 35	+ 18	.....
D. Lymphosarcoma of orbit	133	62	Carcinoma of lacrimal sac	Lymphosarcoma of orbit (lymphocytic-cell)	+ 30 + 89*	+ 74 + 93*	.....
Lid lesions							
A. Metastatic malignant melanoma	16	35	Metastatic malignant melanoma	None	+ 37	+ 48	Primary site, left forearm
B. Chronic granuloma	31	70	Tumor right lower lid margin	Chronic granuloma	+ 7	+ 20	.....
	195	33	Granuloma right lower lid	Granuloma	+ 63	+ 63	.....
C. Pigmented nevus	113	55	Pigmented nevus, left upper and lower lids	None UL† LL†	+ 4 + 14	+ 15 — 2	Probably congenital
D. Squamous-cell epithelioma	144	54	Squamous-cell epithelioma	Same	+293	+228	.....
	179	81	Squamous-cell epithelioma	Same	+111	+126	.....
	227	59	Squamous-cell epithelioma	Same	+129	+128	.....
E. Basal-cell epithelioma	138	42	Basal-cell epithelioma	Same	+161	109	.....
	141	70	Basal-cell epithelioma	Same	+ 61	+ 58	.....
	142	46	Recurrent basal-cell epithelioma	Same	+ 86	+118	.....
	143	84	Recurrent basal-cell epithelioma	Same	+118	+182	.....
	171	62	Recurrent tumor, lower lid	Basal-cell epithelioma	+155	+ 81	.....
	207	55	Recurrent basal-cell epithelioma	Same	+ 51	+ 55	.....
	212	68	Rodent ulcer, left lower lid	Basal-cell epithelioma	+ 72	+151	.....
	259	57	Basal-cell epithelioma	Same	+ 76	+ 83	.....

* Repeat test three months later.
† UL, upper lid; LL, lower lid.

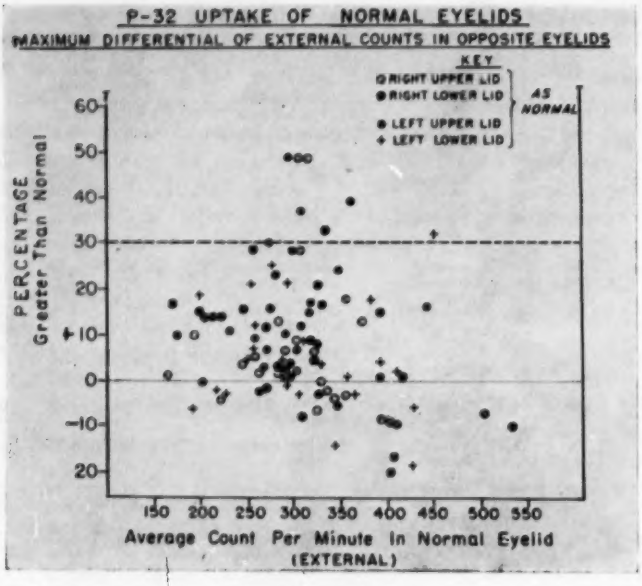


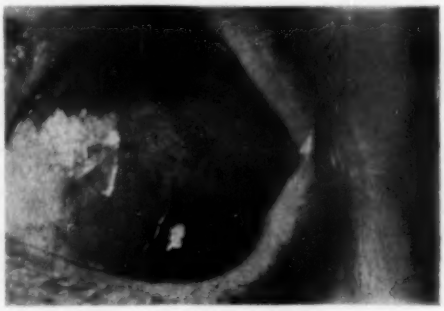
Figure 18

tion, one may calculate the difference in P^{32} uptake as "percentage greater or less than normal." The procedure was then reversed, so that each lid was considered as the normal, or standard. Both upper and both lower lids were included, but calculations were made only with similar lids. Figure 18 shows the results of these calculations. It will be noted that 93% of the calculations fall below 30% greater than normal. This, in effect, parallels the original data of Eisenberg, Leopold, and Sklaroff [7] made on the globe. However, seven determinations lie between 30% and 49% "greater than normal." On the basis of the work of Jones, Chaikoff, and Lawrence [37] and of our own experience in intraocular lesions, it was assumed that tumor tissue would retain enough P^{32}, as compared with normal tissue, that the 24-hour determination would increase beyond the first calculation. Therefore, it was reasoned that any initial count above 30% greater than normal was a significant one, with the reservation that the calculation must rise above the original one in 24 hours to be considered a positive test. As will be seen shortly, these criteria are not applicable in certain lid lesions in which the initial count is over 100% greater than the normal.

B. Results.—I. Conjunctival Lesions: (*a*) Cancerous melanosis of conjunctiva. One patient with cancerous melanosis of the conjunctiva was tested with P^{32}. The test was positive. Figure 19 reveals the external appearance prior to surgery.

(*b*) Pigmented nevus of conjunctiva. Two patients with pigmented nevi of the conjunctiva were tested with P^{32}. In one case the lesion was on the plica semilunaris. Both tests were negative. To date surgery has

Fig. 19 (Case 61).—Cancerous melanosis of conjunctiva.



not been performed in either of these patients.

II. Orbital Lesions: (*a*) Mucocele. Three cases in which the clinical diagnosis was mucocele were tested with P^{32}. The first case (Case 29) revealed a slight uptake of P^{32} initially, with a decrease in 24 hours. Surgery was performed, and an ossifying fibroma of the ethmoid sinus was removed. In the second case (Case 128) the P^{32} uptake was 47% greater than normal in one hour, decreasing in 24 hours. During surgery the lesion ruptured. Pathologic section of the tissue removed revealed a chronic inflammatory reaction. In the third case (Case 162) there was a nodular mass extending from the lateral margin of the orbit, above, to the medial aspect of the orbit. The P^{32} uptake test was negative. Surgery revealed a large mucocele of the frontal sinus.

(*b*) Lacrimal gland inflammation. There were three cases tested in which the clinical diagnosis was tumor of the lacrimal gland. In all three cases a palpable mass was present, so that the end-window of the counter tube was placed over the skin in direct contact with the mass.

Two of these three cases showed only slight uptake of P^{32}. Pathologic examination revealed sarcoid of the lacrimal gland in one case and chronic dacryoadenitis in the other. In the third case (Case 109) there was an extremely high uptake initially, with a subsequent decrease in 24 hours. Pathologic study proved the lesion to be chronic dacryoadenitis.

(*c*) Pseudotumor of the orbit. Two cases of pathologically proved pseudotumor of the orbit were tested with P^{32}. In one case (Case 106) the clinical diagnosis was bilateral herniated fat masses. Pathologic section revealed a granuloma. In the other case (Case 123) the clinical diagnosis was an orbital tumor. Pathologic examination revealed the mass to be a chronic granuloma. The first case showed little P^{32} uptake, while the second case revealed an uptake of 35% greater than normal initially, with a decrease in 24 hours.

(*d*) Lymphosarcoma of the orbit. One case of true orbital tumor was tested with P^{32}. Clinically, the lesion was manifest as a hard nodular mass extending forward to the region of the lacrimal sac. P^{32} uptake was 30% greater than normal initially, with an increase in 24 hours. The patient was urged to have a biopsy, but surgery was delayed for three months. When the patient finally consented to enter the hospital, the mass had enlarged to such an extent that slight pressure produced a marked proptosis. P^{32} uptake studies were repeated and again were positive. Pathologic studies following exeneration of the orbit revealed the mass to be a lymphocytic-cell lymphosarcoma of the orbit with anterior extension.

(*e*) Exophthalmos. One patient with bilateral exophthalmos for whom the diagnosis of thyrotoxicosis was equivocal and two patients with unilateral exophthalmos were subjected to P^{32} uptake study. The test was negative in each case. None of these cases had surgery. Testing in these cases was difficult, since there was no specific mass over which the counter tube could be placed.

III. Lid Lesions: There were 14 lid lesions tested 1 hour and 24 hours after injection with P^{32}. Of these, one was diagnosed clinically as metastatic malignant melanoma; two were proved pathologically to be chronic granulomas, one was clinically diagnosed as a pigmented nevus, three were proved pathologically as squamous-cell epitheliomas, and seven were pathologically proved to be basal-cell epitheliomas.

Counts for the metastatic malignant melanoma of the upper eyelid were performed on the everted lids rather than externally because the lesion appeared to be more extensive internally (Fig. 20). The test in this case was positive.

The tests in both cases of chronic granuloma of the eyelid were negative. The first lesion revealed a low concentration of P^{32}, while the second lesion responded with an uptake of 63% greater than normal in one hour, this value remaining the same for 24 hours.

The test in the case of the pigmented nevus of the eyelids (Fig. 21) showed only a slight uptake of P^{32}, as evidenced by the low calculations.

There was a high initial uptake of P^{32} in each of the three cases of squamous-cell epithelioma. In two of these cases the calculations decreased in 24 hours but remained over 100% greater than normal. Figure 22 shows the squamous-cell carcinoma in Case 144.

Fig. 21 (Case 113).—Pigmented nevus of lids.

Fig. 20 (Case 16).—Metastatic malignant melanoma to eyelid. *A*, external view; *B*, everted lid.

Of the seven cases of basal-cell epithelioma, five revealed an uptake of less than 100% greater than normal in one hour. All but one of these increased the calculation in 24 hours. In two cases the calculations were over 100% greater than normal in one hour, and one of these decreased the calculation in 24 hours. Figure 23 shows the lesion tested in Case 142.

C. Comment.—It is quite evident that from such a small series of extraocular (adnexal) lesions no definite conclusions can be made. However, it appears that in adnexal lesions the results of the test followed a pattern similar to that experienced with intraocular lesions, with the exception of epitheliomas of the lids. In lid lesions, when the one-hour calculation had risen above 100% greater than normal, a decrease in the 24-hour calculation usually occurred. The criteria for positivity in lid lesions were therefore modified so that the test was considered

Fig. 22 (Case 144).—Squamous-cell epithelioma.

Fig. 23 (Case 142).—Recurrent basal-cell epithelioma.

positive when either of the following criteria were present: (1) The one-hour calculation was above 30% greater than normal and the 24-hour calculation increased beyond the original one, or (2) the original one-hour calculation was over 100% greater than normal.

When these new criteria are applied to lid lesions, it is seen that all three cases of squamous-cell epithelioma had positive tests, while six of the seven tests for basal-cell epithelioma were positive.

It appears that in certain cases normal lid tissues, including skin, do not excrete their initial concentration of P^{32} rapidly enough so that in 24 hours a good differential between malignancy and normal lid occurs.

There are many variables encountered in testing extraocular (adnexal) lesions with P^{32}. Factors such as size and vascularity of the lesion, thickness of the normal tissue overlying the tumor, and tissue thickness and vascularity of the site used as the normal for comparison, all may be included. The variables of tumor growth and phosphorus metabolism must also be included, for it is well known that certain malignancies, such as basal-cell epithelioma, are comparatively very slow in growth; consequently, it would be expected that the phosphorus metabolism of such tumors would generally be lower than that of tumors characterized by more rapid growth.

In certain adnexal lesions, P^{32} testing prior to surgery occasionally offers the surgeon an advantage otherwise attainable only by biopsy. With lid lesions, however, the test does not offer as great an advantage, for most of these are easily accessible to biopsy or surgical excision without risk of tumor spread, as could occur with biopsy of an orbital mass.

SUMMARY AND CONCLUSIONS

A total of 262 cases of ocular pathology in which P^{32} uptake studies were performed are presented. Of these, 233 cases had intraocular lesions, while 29 cases had extraocular (adnexal) lesions. The test was modified to include readings 1 hour and 24 hours after injection of the isotope. A new criterion for positivity was established. The test is considered positive when in one hour there is an uptake over 30% greater than the normal and in 24 hours there is an increase beyond the one-hour calculation. In lid lesions, the above criteria are applicable, but the test is also considered positive if the one-hour calculation is over 100% greater than normal regardless of the 24-hour calculation.

In the 233 cases of intraocular lesions subjected to P^{32} uptake testing, there were 3 false-positive tests in the group of inflammatory lesions and 3 false-negative tests in the series of 30 cases of intraocular malignant melanoma. In four other cases of intraocular malignant melanoma repeat tests were performed where the clincal diagnosis was obvious and the P^{32} uptake test had been negative. All of the repeat tests were positive. Three of these occurred in cases where the lesion was posterior to the equator of the globe, while one occurred in a lesion anterior to the equator.

There were five false-negative tests in the series of six cases of retinoblastoma.

Of the 29 cases of extraocular (adnexal) lesions there was one false-negative test occurring in a case of basal-cell epithelioma of the eyelid.

On the basis of our studies, and in the light of the experimental work of other investigators, the following conclusions appear valid:

1. P^{32} uptake studies are a valuable aid in the differential diagnosis of intraocular pathology, especially in the differentiation of serous and solid detachments of the retina, provided that the lesion is within reach of the counter tube.

2. Intraocular malignancy in the posterior segment of the globe beyond the reach of the presently used counter tube gives equivocal results when tested with P^{32}.

3. The P^{32} uptake test gives less accurate results in intraocular cases involving patients with one eye, in cases of bilateral ocular pathology, and in cases in which previous

intraocular surgery has created a state of inflammatory reaction.

4. For reasons yet unknown, the P^{32} test as performed in this laboratory is decidedly reduced in accuracy in cases of retinoblastoma.

5. In this study, no correlation could be made between the P^{32} uptake measured in vivo as "per cent greater than normal" and the cellular type of the malignant melanoma studied in vitro following enucleation.

6. In extraocular (adnexal) lesions the results of the test appear to follow a pattern similar to that experienced with intraocular lesions, with the exception of epitheliomas of the eyelids.

7. P^{32} testing prior to surgery in certain adnexal lesions occasionally offers the surgeon an advantage otherwise attainable only by biopsy. In lid lesions the test does not offer as great an advantage.

8. The validity of the P^{32} uptake test depends upon (1) the ability of malignant tissue to concentrate P^{32}, (2) the capacity of malignant tumor tissue to retain P^{32} over a period of time, and (3) the faculty of normal tissues to excrete their initial concentration of P^{32} rapidly.

The Attending Surgeons and members of the staff of the Wills Eye Hospital cooperated in this study. Dr. John McGavic, pathologist to the Wills Eye Hospital, and his staff made the pathologic diagnoses. Miss A. Bilyi made the photographs.

1601 Spring Garden St.

REFERENCES

1. Thomas, C. I.; Krohmer, J. S., and Storaasli, J. P.: Detection of Intraocular Tumors with Radioactive Phosphorus, A. M. A. Arch. Ophth. **47**:276, 1952.

2. Thomas, C. I.; Krohmer, J. S.; Storaasli, J. P., and Friedell, H. L.: Detection of Intraocular Tumors by the Use of Radioactive Phosphorus, Am. J. Ophth. **38**:93, 1954.

3. Town, A. E.: Differential Diagnosis Between Solid and Serous Detachment of the Retina, Pennsylvania M. J. **56**:1046, 1953.

4. Town, A. E.: Radioactive Phosphorus Studies in the Diagnosis of Ocular Tumors: A Preliminary Report, West Virginia M. J. **48**:356, 1952.

5. Dunphy, E. B., and Selverstone, B.: Uptake of Radioactive Phosphorus by Normal and Neoplastic Ocular Tissues, Am. J. Ophth. **36**:774, 1953.

6. Dunphy, E. B.; Dreisler, K. K.; Cadigan, J. B., and Sweet, W.: The Uptake of Radioactive Phosphorus by Intraocular Neoplasms, Am. J. Ophth. **37**:45, 1954.

7. Eisenberg, I. J.; Leopold, I. H., and Sklaroff, D.: Use of Radioactive Phosphorus in Detection of Intraocular Neoplasms, A. M. A. Arch. Ophth. **51**:633, 1954.

8. Eisenberg, I. J.; Terner, I. S., and Leopold, I. H.: Use of P^{32} as an Aid in Diagnosis of Intraocular Neoplasms, A. M. A. Arch. Ophth. **52**:741, 1954.

9. Kennedy, R. J.; Glasser, O., and Kazdan, P.: The Use of Radioactive Phosphorus in the Detection of Intraocular Tumors, Cleveland Clin. Quart. **21**:133, 1954.

10. Curie, I., and Joliot, F.: Artificial Production of a New Kind of Radioelement, Nature **133**:201, 1934.

11. Lawrence, E. O., and Cooksey, D.: On the Apparatus for the Multiple Acceleration of Light Ions to High Speeds, Physical Rev. **50**:1131, 1936.

12. Lawrence, E. O., and others: Initial Performance of the 60-Inch Cyclotron of the William H. Crocker Radiation Laboratory of the University of California, Physical Rev. **56**:124, 1939.

13. Lawrence, E. O.: The Medical Cyclotron of the William H. Crocker Radiation Laboratory, Science **90**:407, 1939.

14. Aebersold, P. C.: Survey of Isotope Utilization in the Study and Treatment of Cancer, Acta Unio internat. contra cancrum **9**:19, 1953

15. Hamilton, J. G.: The Use of Radioactive Tracers in Biology and Medicine, Radiology **39**: 541, 1942.

16. Hevesy, G.: The Absorption and Translocation of Lead by Plants: A Contribution to the Application of the Method of Radioactive Indicators in the Investigation of the Change of Substance in Plants, Biochem. J. **17**:439, 1923.

17. Chiewitz, O., and Hevesy, G.: Radioactive Indicators in the Study of Phosphorus Metabolism in Rats, Nature **136**:754, 1935.

18. Lawrence, J. H., and Scott, K. G.: Comparative Metabolism of Phosphorus in Normal and Lymphomatous Animals, Proc. Soc. Exper. Biol. & Med. **40**:694, 1939.

19. Lawrence, J. H.; Scott, K. G., and Tuttle, L. W.: Studies on Leukemia with the Aid of Radioactive Phosphorus, Internat. Clin. **3**:33, 1939.

20. Lawrence, J. H.; Tuttle, L. W.; Scott, K. G., and Connor, C. L.: Studies on Neoplasms with the Aid of Radioactive Phosphorus: I. The Total Phosphorus Metabolism of Normal and Leukemic Mice, J. Clin. Invest. **19**:267, 1940.

21. Tuttle, L. W.; Erf, L. A., and Lawrence, J. H.: Studies on Neoplasms with the Aid of Radioactive Phosphorus: II. The Phosphorus Metabolism of the Nucleoprotein, Phospholipid, and Acid Soluble Fractions of Normal and Leukemic Mice, J. Clin. Invest. **20**:57, 1941.

22. Tuttle, L. W.; Erf, L. A., and Lawrence, J. H.: Studies on Neoplasms with the Aid of Radioactive Phosphorus: III. The Phosphorus Metabolism of the Phospholipid, Acid Soluble, and Nucleoprotein Fractions of Various Tissues of Normal and Leukemic Mice Following the Administration of "Tracer" and "Therapeutic" Doses of Radiophosphorus, J. Clin. Invest. **20**:577, 1941.

23. Tuttle, L. W.; Scott, K. G., and Lawrence, J. H.: Phosphorus Metabolism in Leukemic Blood, Proc. Soc. Exper. Biol. & Med. **41**:20, 1939.

24. Erf, L. A.; Tuttle, L. W., and Scott, K. G.: Retention of Orally Administered Radiophosphorus by Mice, Proc. Soc. Exper. Biol. & Med. **45**:652, 1940.

25. Erf, L. A., and Lawrence, J. H.: Clinical Studies with the Aid of Radioactive Phosphorus: I. The Absorption and Distribution of Radio-Phosphorus in the Blood and Its Excretion by Normal Individuals and Patients with Leukemia, J. Clin. Invest. **20**:567, 1941.

26. Erf, L. A., and Lawrence, J. H.: Clinical Studies with the Aid of Radiophosphorus: VI. The Absorption and Distribution of Radio-Phosphorus in the Blood of, Its Excretion by, and Its Therapeutic Effect on, Patients with Polycythemia, Ann. Int. Med. **15**:277, 1941.

27. Erf, L. A., and Lawrence, J. H.: Phosphorus Metabolism in Neoplastic Tissue, Proc. Soc. Exper. Biol. & Med. **46**:694, 1941.

28. Erf, L. A.: Retention of Radiophosphorus in Whole and Aliquot Portions of Tissues of Patients Dead of Leukemia, Proc. Soc. Exper. Biol. & Med. **47**:287, 1941.

29. Lawrence, J. H.: Preliminary Report on a New Method for the Treatment of Leukemia and Polycythemia, Radiology **35**:51, 1940.

30. Lawrence, J. H.: Observations on the Nature and Treatment of Leukemia and Allied Diseases, Proc. Inst. Med. Chicago **14**:30, 1942.

31. Lawrence, J. H.: Nuclear Physics and Therapy: Preliminary Report on a New Method for the Treatment of Leukemia and Polycythemia, Radiology **35**:51, 1940.

32. Marshak, A.: Uptake of Radioactive Phosphorus by Nuclei of Liver and Tumors, Science **92**:460, 1940.

33. Marshak, A.: P^{32} Uptake by Nuclei, J. Gen. Physiol. **25**:275, 1941.

34. Jones, H. B.; Chaikoff, I. L., and Lawrence, J. H.: Radioactive Phosphorus as an Indicator of Phospholipid Metabolism: VI. The Phospholipid Metabolism of Neoplastic Tissues (Mammary Carcinoma, Lymphoma, Lymphosarcoma, Sarcoma 180), J. Biol. Chem. **128**:631, 1939.

35. Jones, H. B.; Chiakoff, I. L., and Lawrence, J. H.: Radioactive Phosphorus as an Indicator of Phospholipid Metabolism: The Phospholipid Turnover of Fraternal Tumors, J. Biol. Chem. **133**:319, 1940.

36. Jones, H. B.; Chiakoff, I. L., and Lawrence, J. H.: Phosphorus Metabolism of the Soft Tissues of the Normal Mouse as Indicated by Radioactive Phosphorus, Am. J. Cancer **40**:235, 1940.

37. Jones, H. B.; Chiakoff, I. L., and Lawrence, J. H.: Phosphorus Metabolism of Neoplastic Tissues (Mammary Carcinoma, Lymphoma, Lymphosarcoma) as Indicated by Radioactive Phosphorus, Am. J. Cancer **40**:243, 1940.

38. Schulman, J.; Falkenheim, M., and Gray, S. J.: The Phosphorus Turnover of Carcinoma of the Human Stomach as Measured with Radioactive Phosphorus, J. Clin. Invest. **28**:66, 1949.

39. Marinelli, L. D., and Goldschmidt, B.: The Concentration of P^{32} in Some Superficial Tissues of Living Patients, Radiology **39**:454, 1942.

40. Low-Beer, B. V. A.: Surface Measurements of Radioactive Phosphorus in Breast Tumors as a Possible Diagnostic Method, Science **104**:399, 1946.

41. Low-Beer, B. V. A.; Bell, H. G.; McCorckle, H. J.; Stone, R. S.; Steinbach, H. L., and Hill, W. B.: The Measurement of Radioactive Phosphorus in Breast Tumors in Situ: A Possible Diagnostic Procedure, Radiology **47**:492, 1946.

42. McCorckle, H. J.; Low-Beer, B. V. A.; Bell, H. G., and Stone, R. S.: Clinical and Laboratory Studies on the Uptake of Radioactive Phosphorus by Lesions of the Breast, Surgery **24**:409, 1948.

43. Herly, L.: Studies in Selective Differentiations of Tissues by Means of Filtered Ultraviolet Light, Cancer Res. **4**:227, 1944.

44. Moore, G. E.: Fluorescein as an Agent in the Differentiation of Normal and Malignant Tissues, Science **106**:130, 1947.

45. Moore, G. E.; Hunter, S. W., and Hubbard, T. B.: Clinical and Experimental Studies of Fluorescein Dyes with Special Reference to Their Use for the Diagnosis of Central Nervous System Tumors, Ann. Surg. **130**:637, 1949.

46. Moore, G. E.: The Use of Radioactive Diiodofluorescein in the Diagnosis and Localization of Brain Tumors, Science **107**:569, 1948.

47. Moore, G. E.; Peyton, W. T.; French, L. A., and Walker, W. W.: The Clinical Use of Fluorescein in Neurosurgery: The Localization of Brain Tumors, J. Neurosurg. **5**:392, 1948.

48. Moore, G. E.; Peyton, W. T.; Hunter, S. W., and French, L.: The Clinical Use of Sodium Fluorescein and Radioactive Diiodofluorescein in the Localization of Tumors of the Central Nervous System, Minnesota Med. **31**:1073, 1948.

49. Marvin, J. F., and Moore, G. E.: Localization of Brain Tumors with Radioiodyes: 2. Experimental Evaluation of the Physical Limitations, Nucleonics **3**:52, 1948.

50. Moore, G. E.; Kohl, D. A.; Marvin, J. F.; Wong, J. C., and Caudill, C. M.: Biophysical Studies of Methods Utilizing Fluorescein and Its Derivatives to Diagnose Brain Tumors, Radiology **55**:344, 1950.

51. Moore, G. E.; Caudill, C. M.; Marvin, J. F.; Aust, J. B.; Chou, S. N., and Smith, G. A.: Clinical and Experimental Studies of Intracranial Tumors with Fluorescein Dyes with an Additional Note Concerning the Possible Use of K^{42} and $Iodine^{131}$ Tagged Human Albumin, Am. J. Roentgenol. **66**:1, 1951.

52. Chou, S. N.; Moore, G. E., and Marvin, J. F.: Localization of Brain Tumors with Radioiodine, Science **115**:119, 1952.

53. Ashkenazy, M.; LeRoy, G. V.; Fields, T., and Davis, L.: The Detection of Intracranial Tumors by the Use of Di-Iodofluorescein, J. Lab. & Clin. Med. **34**:1580, 1949.

54. Davis, L.; Martin, J.; Ashkenazy, M.; LeRoy, G. V., and Field, T.: Radioactive Diiodofluorescein in Diagnosis and Localization of Central Nervous System Tumors, J. A. M. A. **144**:1424, 1950.

55. Selverstone, B., and Solomon, A. K.: Radioactive Isotopes in the Study of Intracranial Tumors, Tr. Am. Neurol. A. **73**:115, 1948.

56. Selverstone, B.; Solomon, A. K., and Sweet, W. H.: Location of Brain Tumors by Means of Radioactive Phosphorus, J. A. M. A. **140**:277, 1949.

57. Selverstone, B.; Sweet, W. H., and Robinson, C. V.: The Clinical Use of Radioactive Phosphorus in the Surgery of Brain Tumors, Ann. Surg. **130**:643, 1949.

58. Roswit, B.; Sorrentino, J., and Yalow, R.: The Use of Radioactive Phosphorus (P^{32}) in the Diagnosis of Testicular Tumors: A Preliminary Report, J. Urol. **37**:724, 1950.

59. Trevor-Roper, P. D.; Newton, K. A., and Nicholson, J. P.: Radioactive Diiodofluorescein in the Diagnosis of Intra-Ocular Tumors, Brit. J. Ophth. **36**:543, 1952.

60. Bettman, J. W., and Fellows, V.: Radioactive Phosphorus as a Diagnostic Aid in Ophthalmology, A. M. A. Arch. Ophth. **51**:171, 1954.

61. Snodgrass, M. B.; Lenihan, J., and Primrose, D. A.: Radioactive Phosphorus as an Aid to the Diagnosis of Malignant Melanoma of the Eye, Brit. J. Ophth. **38**:553, 1954.

62. Kenny, J. M.; Marinelli, L. D., and Craver, L. F.: The Treatment of Lymphosarcoma with Radioactive Phosphorus: A Preliminary Report, Am. J. Roentgenol. **47**:217, 1942.

63. Reinhard, E. H.; Moore, C. V.; Bierbaum, O. S., and Moore, S.: Radioactive Phosphorus as a Therapeutic Agent: A Review of the Literature and Analysis of the Results of Treatment of 155 Patients with Various Blood Dyscrasias, Lymphomas, and Other Malignant Neoplastic Diseases, J. Lab. & Clin. Med. **31**:107, 1946.

64. Forssberg, A.: A Study of the Distribution of Radioactive Phosphorus in 3 Cases of Cancer, Acta radiol. **27**:88, 1945.

65. Forssberg, A., and Jacobsson, F.: Studies on the Brown-Pearce Rabbit-Carcinoma with the Aid of Radioactive Isotopes, Acta radiol. **26**:523, 1945.

66. Friedell, H. L., and Storaasli, J. P.: The Use of Radioactive Phosphorus in the Treatment of Carcinoma of the Breast with Widespread Metastasis to Bone, Am. J. Roentgenol. **64**:559, 1950.

67. Hertz, S.: Modifying Effect of Steroid Hormone Therapy of Human Neoplastic Disease as Judged by Radioactive Phosphorus (P^{32}) Studies, J. Clin. Invest. **29**:821, 1950.

68. Erickson, T. C.; Larson, F., and Gordon, E. S.: Uptake of Radioactive Phosphorus by Glioblastoma Multiforme and Therapeutic Application, Tr. Am. Neurol. A. **73**:712, 1948.

69. Sweet, W. H.: The Uses of Nuclear Disintegration in the Diagnosis and Treatment of Brain Tumors, New England J. Med. **245**:875, 1951.

70. Brucer, M.: Encouraging and Discouraging Research with Therapeutic Radioisotopes, J. Kentucky M. A. **51**:243, 1953.

71. Marinelli, L. D., and Kenney, J. M.: The Absorption of Radiophosphorus in Irradiated and Non-Irradiated Mice, Radiology **37**:691, 1941.

72. Allen, H.; Hempelmann, L. H., Jr., and Wornach, N. A.: The Effect of Insoluble Radiophosphorus (Chromium Phosphate) When Applied Interstitially in the Treatment of Adenocarcinoma of the Mamma in Mice, Cancer Res. **5**:239, 1945.

73. Low-Beer, B. V. A.: Radioactive Phosphorus as an External Therapeutic Agent in Basal Cell Carcinoma, Warts, and Hemangioma, Am. J. Roentgenol. **58**:4, 1947.

74. Kruger, P. G.: Some Biological Effects of Nuclear Disintegration Products on Neoplastic Tissue, Proc. Nat. Acad. Sc. **26**:181, 1940.

75. Zahl, P. A.; Cooper, F. S., and Dunning, J. R.: Some in Vivo Effects of Localized Nuclear Disintegration Products on a Transplanted Mouse Sarcoma, Proc. Nat. Acad. Sc. **26**:586, 1940.

76. Sweet, W. H., and Javid, M.: The Possible Use of Slow Neutrons Plus $Boron^{10}$ in Therapy of Intracranial Tumors, Tr. Am. Neurol. A. **76**:60, 1951.

77. Farr, L. E., and others: Neutron Capture Therapy with Boron in the Treatment of Glioblastoma Multiforme, Am. J. Roentgenol. **71**:279, 1954.

78. Wolff, E.: The Anatomy of the Eye and Orbit, Ed. 3, Philadelphia, The Blakiston Company, 1951, p. 212.

79. Thomas, C. I.; Krohmer, J. S., and Storaasli, J. P.: Geiger Counter Probe for Diagnosis and Localization of Posterior Intraocular Tumors, A. M. A. Arch. Ophth. **52**:413, 1954.

80. Duke-Elder, S.: Text-Book of Ophthalmology, Vol. III, St. Louis, C. V. Mosby Company, 1945, p. 2514.

81. Erdbrink, W. L., and Harbert, F.: Leiomyoma of the Iris, A. M. A. Arch. Ophth. **53**:643. 1955.

Further Studies of Effects of X-Radiation on Partially Shielded Lens of Rabbit

P. J. LEINFELDER, M.D.
and
E. F. RILEY, Ph.D., Iowa City

Previous experiments by one of us (P. J. L.) in 1953 [1] have demonstrated that the irradiation of one quadrant of the lens with x-rays results in opacity limited to the area of exposure. In our original work low doses were used and incomplete cataract resulted. More recently, in an attempt to produce rapidly an overwhelming effect in one sector of the lens, considerably larger doses of radiation were utilized.

EXPERIMENTAL STUDY

Albino rabbits of approximately 2 kg. were used in the experiments. X-ray exposure factors were 200 kv., 5 ma., 27 cm. distance, 150 r per minute, and 1 mm. Al filtration. Single exposures measured in air with a Victoreen r-meter were employed. Exposure of the lens was limited by lead shield (Fig. 1), sutured to the sclera of the anesthetized rabbit. Further shielding was obtained by covering the remainder of the animal with sheet lead. One quadrant of the lens of eight animals was irradiated with a dose of 1,000 to 11,800 r. The lens quadrant of four of these animals received more than 5000 r. Two lens quadrants in one eye of four rabbits were exposed to a dose of 5,000 to 12,000 r.

Lens Quadrants Irradiated and Dose

Quadrants Exposed	No. of Animals	Dose, r
1	1	1,000
1	1	3,000
1	1	4,700
1	2	5,000
1	1	10,000
1	1	11,800
2	1	3,000
2	1	5,000
2	1	7,500
2	2	12,000

RESULTS

Lens opacities occurred in the exposed area of all the irradiated eyes after a latent period that varied from approximately two

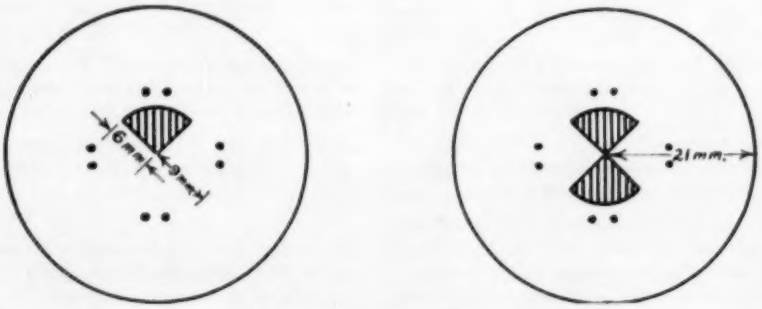


Fig. 1.—Lead shield for partial irradiation of the lens.

Received for publication Oct. 17, 1955.

This paper is based on work done under Contract AT (11-1)72 Project I, for the U. S. Atomic Energy Commission.

Department of Ophthalmology, State University of Iowa College of Medicine (Dr. Leinfelder). Radiation Research Laboratory, State University of Iowa College of Medicine (Dr. Riley).

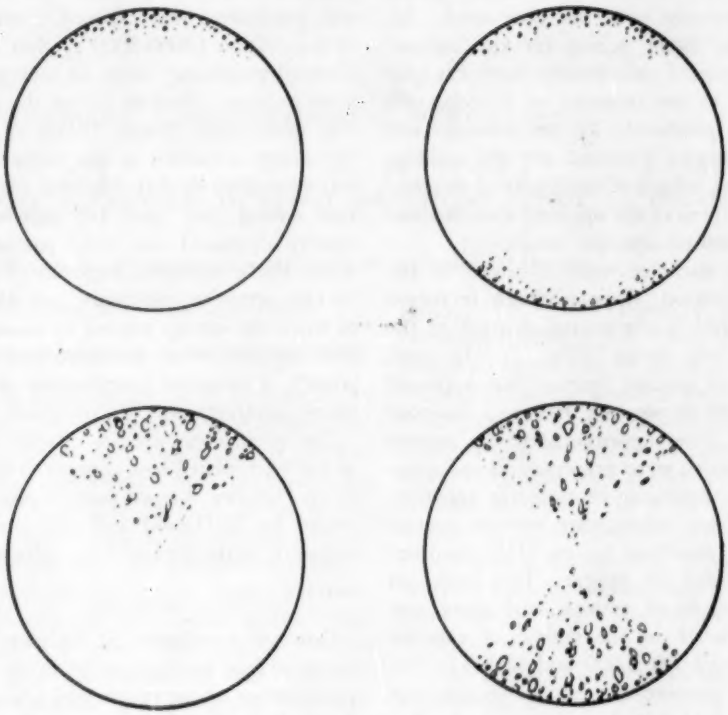
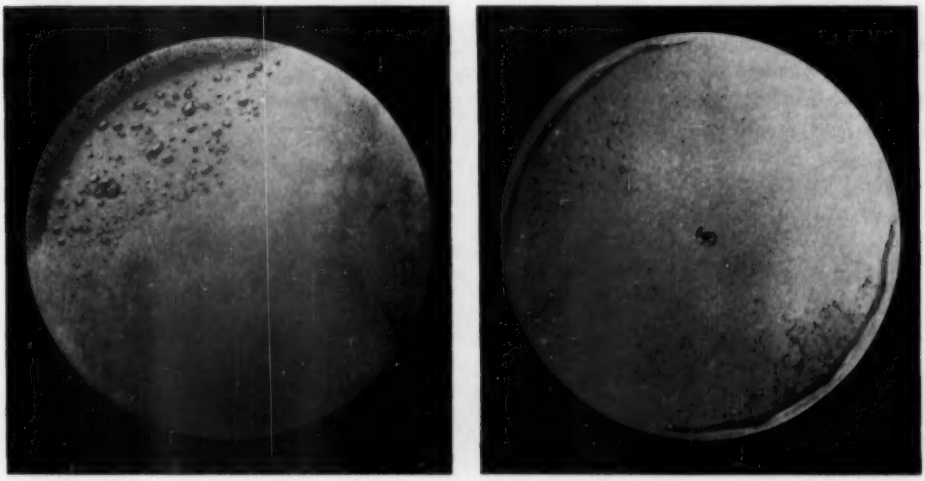


Fig. 2.—Early and late effects of irradiation of one and two quadrants of the lens.

Fig. 3.—Drawing showing vacuoles and arcuate opacity in exposed quadrants of the rabbit lens.



weeks to six months. The latent period varied inversely with the dose used. Although the latent period for the cataract formation varied considerably, there was little difference in the intensity of the opacities ultimately produced. In no instance was complete opacity observed, nor did opacities occur in the untreated quadrants of the lens. In all but three of the opposite eyes minimal posterior sutural opacities occurred.

Initially vacuoles were observed in the equatorial region; these gradually increased and appeared in the central portion of the posterior lens cortex (Fig. 2). In most instances an arcuate opacity that appeared to be in the perinuclear area was observed (Fig. 3). After approximately six months fewer vacuoles were present, and the arcuate opacity gradually became less apparent. The posterior subcapsular sutural opacity previously described by us after quadrant irradiation did not appear. This evolution was noticed in all animals, and there was little difference in the degree of cataract produced by 3,000, 5,000, and 12,000 r. The difference between one- and two-quadrant irradiation was only that of two areas being involved rather than one.

COMMENT

These experiments suggest that, when two or three quadrants of the lens are shielded from the injury of x-radiation, the protected portions may somehow prevent the progression to a complete radiation cataract. Only a partial opacity in the exposed area was observed when one quadrant (or two opposite quadrants) was exposed to an amount of x-radiation (3000-5000 r) that produced a complete cataract when all four quadrants were exposed. Further, when the exposure was quadrupled (about 12,000 r), so that the energy absorbed in the single quadrant was equivalent to that absorbed in the entire lens during four quadrant exposures, the opacity produced was only partial. Even when the quadrupled exposure was given to two opposite quadrants (an absorption of twice the energy needed to cause a complete cataract when an entire lens was exposed), a complete opacification of the exposed quadrants was not observed.

The perinuclear arcuate opacity observed in the x-irradiated lens appears to be similar to the "crescent-shaped shadow opacity" observed by McDonald and associates [2] after exposure of the lens to beta radiation.

SUMMARY

Doses of x-radiation as high as 12,000 r produced only partial cataract in the exposed quadrant(s) of the rabbit lens when two or three of the lens quadrants were shielded from the radiation.

REFERENCES

1. Alter, A. J., and Leinfelder, P. J.: Roentgen X-Ray Cataract Effects of Shielding of the Lens and Ciliary Body, A. M. A. Arch. Ophth. **49**:257-260 (March) 1953.

2. McDonald, J. E.; Hughes, W. F., Jr., and Peiffer, V. G.: Beta Radiation Cataracts, A. M. A. Arch. Ophth. **53**:248-258 (Feb.) 1955.

Permanent Convergent Squint — Early Operation and Long-Term Follow-Up

A Contribution to the Elucidation of the Mechanism of Development of Esotropia

W. NORDLÖW, M.D., Vänersborg, Sweden

The primary object of this paper is to account for the relative position of the eyes, binocular vision, and visual acuity in cases of permanent convergent squint operated upon early and thereafter followed up for a prolonged period. These cases did not undergo orthoptic training. By orthoptic training is understood, in the present paper, exercises to counteract the suppression of the image from the one eye, abolishing anomalous retinal correspondence and any incorrect relation between accommodation and convergence, and the use of prismatic lenses for improvement of the amplitude of fusion or compensation of the angle of squint.

This investigation may, further, be regarded as a contribution to a more comprehensive task, viz., the elucidation of the mechanism of the development of esotropia. In this respect it is complementary to previous publications by me (Nordlöw * and Dahlberg and Nordlöw [2]). This aspect will be considered further in "Comment."

REVIEW OF THE LITERATURE

Several authors have proposed early operation for squint without, however, accounting for personal material, e. g., Wiesinger [25] (1906), Rønne [22] (1910), and Dunnington [4] (1933). Other authors have attempted the procedure in isolated or in a few cases, e. g., Priestley Smith [23] (1899), Pollock [15] (1921), Lowell [9] (1926), Bettremieux [3] (1927), Hepburn [7] (1932), Peter [17] (1932), and Forsmark [6] (1932). In 1940, Mügge [10] reported 20 cases. The object of the operation differed somewhat with the various authors. In all papers the information supplied is inadequate and the period of observation too short to enable the reader personally to evaluate the results. In a few cases the advantage of early operation over operation at a later date is not obvious. When adults are operated upon, some cases may happen to acquire correct positioning of the eyes with binocular vision.

With the establishment of more convincing criteria for the significance of the mechanical factor in the development of esotropia (Nordlöw,[11] 1942), early operation appeared more justified. In 1945, I [12] published my first personal material of patients suffering from permanent convergent squint who were operated upon early and were not trained orthoptically. The material comprised 17 cases collected at random and 5 cases selected on the basis of age. The technique of investigation and operation and the results are stated in detail. Of the cases in which the squint developed after the first 6 months of life and which were observed from 7 months until 3 years, 20 acquired binocular fixation (see "Method," Point 5 *a*). Of 10 cases which could be investigated in more detail, 8 showed good stereoscopic vision and normal amplitude of fusion.

Early operation has been attempted also by other authors, e. g., by Exnerovâ [5] (1948). Stanworth [24] (1949) accounts for 100 selected cases in which orthoptic training revealed that binocular single vision could not be obtained. After operation within four

Received for publication Aug. 31, 1955.

* References 11, 12, 14, and 15.

years after the development of the squint, 26 cases acquired fusion, while 20 of these acquired stereoscopic vision.

Early operation without orthoptic training was also studied by Riise [20] (1953) in 28 cases, by Huggert [8] (1954), and by Rønne [21] (1954) in 153 cases, among others. This material was followed up for five to six years but is not representative, as *inter alia*, cases with amblyopia of more than 6/18 were excluded. Whether cases of intermittent squint are included is not recorded. "Normal function" was obtained in 102 cases.

METHODS

In the investigation and treatment of the collected material and in the analysis of the results obtained, the methods and the errors of the methods stated below were employed (Nordlöw †).

1. *Determination of Visual Acuity.*—With children up to the age of 3 years, the ability to fixate and the mode of fixating a small lamp were employed. The child was made to fixate a small lamp placed immediately under one of the investigator's eyes. The examination was carried out at a distance of approximately 0.5 meter. The child's fixating eye was quickly covered, e. g., by the thumb of one hand. If the squinting eye then made a quick adjusting movement toward the lamp and continued to fixate it, that eye was regarded as possessing central fixation. A general requirement prior to operation was that the squinting eye maintain its fixation some seconds or longer after the covering of the good eye had been discontinued. The extent to which this method can insure good or satisfactory visual acuity prior to operation in children under the age of 3 or 4 years can only be decided by determining the visual acuity when the child is older and comparing with cases in which operation was not done. This condition will be discussed in connection with the account of the results. In children at the age of 3 to 4 years, the visual acuity was determined by Henrik Sjögren's (1939) charts; at the age of 4-8 years, more exactly by Boström's ‡ charts, and in children older than this, by Monoyer's chart.

2. *Determination of Refraction.*—Prior to the age of 8 years refraction was performed by means of skiascopy following the instillation of 1% atropine sulfate drops for three days. The readings were carried out with an exactitude of 0.25 D. and were repeated at intervals of one to two years. The refraction obtained by skiascopy when no astigmatism was present corresponds to an optical adjustment of the eye without accommodation within the limits of ±0.66 D. in 77% of the cases. In the remaining 23% the refraction obtained by skiascopy is somewhat more hypermetropic. When astigmatism was present, the limits mentioned above became ±0.75 D. (Nordlöw [13]). In children past the age of 8 years, refraction was determined, in addition, by Donders' method.

3. *Determination of Angle of Squint.*—Prior to operation this was measured on a perimeter, and always at a distance of 5 meters, with correction for the error of refraction of the fixating eye, the primary static angle of squint. Occasionally, the static angle of squint was determined also at a distance of 0.33 meter. The standard error for a single determination of the angle of squint by this method was calculated to be ±0.74°. The limits of the real value thus become ±2.2° (Nordlöw [11]). Alterations in the method stated were made when young children were concerned and it was required to place the center of torsion of the squinting eye at the center of the perimeter in the horizontal plane. The middle of the head support was placed half the pupillary distance lateral to the center of the perimeter. The child's head was held in the head support by an assistant. By means of double determinations at intervals of a few days on 30 children chosen at random, the standard error of a single determination by this method was calculated as ±1.26°. At the limits $\pm 3\sigma$ the limits of the real value become ±3.8°.

4. *Determination of Heterophoria.*—This was undertaken after confirmation of binocular fixation (see Point 5a) and correction of possible errors of refraction. The heterophoria was partly estimated at 0.5 meter; partly, in older children, it was at 5 meters and 0.5 meter by Herschel's double prism, and for long distances by a synoptophore as well. On estimation of the heterophoria, the child's eyes, which were fixating a point of light placed in front of the examiner's eye, were alternately covered. On uncovering the eye, the position of the light reflex in the pupil and the extent of the adjusting movement of the eye were observed. To determine its value (see "Results") this method was employed in conjunction with Herschel's double prism and the synoptophore. For Herschel's double prism and a control material of normal children, the standard error of a single determination was calculated as ±0.59°. The limits of the real value thus become ±1.8° (Nordlöw [11]).

5. *Determination of Presence and Quality of Binocular Vision.*—(*a*) Binocular fixation, (*b*) fusion of simple figures, (*c*) stereoscopic vision,

† References 11, 12, and 13.

‡ Published by Nordiska Bokhandelns Förlagsaktiebolag, Stockholm.

(*d*) amplitude of fusion, and (*e*) retinal correspondence were determined.

(*a*) Binocular fixation (the cover-uncover test) was carried out at 0.5 meter in the following way after the correction of errors of refraction: The child was placed in front of the examiner and was made to fixate a small lamp placed immediately below the examiner's eye. The position of the corneal reflex in relation to the margin of the pupil was recorded. One eye was thereafter covered. If the other eye did not then make any adjusting movement, it was considered to be in the position of fixation. The first eye was then uncovered. If this eye then made an adjusting movement, whereas the other eye remained stationary during the test, this result was interpreted as binocular fixation, probably with some amplitude of fusion. If the covered eye remained stationary on being uncovered, the other eye was rapidly covered. If the first eye still remained stationary, binocular fixation was regarded as present. If it made an adjusting movement, the case was registered as squinting. The extent to which this "binocular fixation" on the occasion of examination corresponds to binocular single vision, and later in life to more or less developed binocular vision, will be discussed in the section on "Results." Following surgery, a period of observation of two to four months has been set for the determination of the presence of binocular fixation.

(*b*) Fusion of simple figures, (*c*) stereoscopic vision, and (*d*) amplitude of fusion were examined on the same synoptophore and in a manner similar to that in previous investigations (Nordlöw §), and the results are therefore comparable. After correction of errors of refraction, the position of equilibrium of the eyes was determined by spider 3×7 mm. and net 25×25 mm. in size, and occasionally also with two points. In this position, fusion was tested by suitable pictures. Stereoscopic vision was tested by four squares in a field of 16×21 mm. The amplitude of fusion was tested by the letters *L* and *F*, 12×15 mm. in size. These, when fused, form *E*. Amplitude of fusion was tested in the following sequence and directions:

from position of equilibrium outward ($5.0° \pm 0.13°$)

inward toward position of equilibrium ($1.6° \pm 0.11°$ and $1.3° \pm 0.12°$)

from position of equilibrium inward without accommodation ($6.7° \pm 0.28°$)

from position of equilibrium inward with accommodation ($16.7° \pm 0.83°$)

outward toward position of equilibrium ($3.9° \pm 0.33°$)

The examination was carried out twice on each occasion, and the average values were employed in the analysis. The normal values, obtained in a similar way, are stated in parentheses (Nordlöw [11]).

(*e*) In examination of retinal correspondence with central after-images, the patient had to fixate the midpoint of an 18-cm. long filament in a tubular lamp at a distance of 1 meter with each eye in turn. The exposure took place in a darkroom and lasted 20 seconds for each eye, and some seconds longer in cases of amblyopia. For the one eye the lamp was placed vertically, and for the other, horizontally. Since the positive or negative after-images could be perceived simultaneously, the patient was asked to draw their relative positions on a piece of paper. The decision concerned normal or anomalous retinal correspondence, i. e., qualitative attributes. Even under such circumstances the method is impaired by possibilities of error. In some cases normal, as well as anomalous, correspondence exists. It may then occur that only one becomes evident at examination. To be certain in all cases, two or more determinations should be performed, at intervals.

6. *Treatment.*—Refractive errors were corrected from the age of 1½ to 2 years. The lenses prescribed were 0.50 D. weaker that the skiascopic refraction to avoid overcorrection (see Point 2). This implies that a number of cases were undercorrected by 0.50-1.25 D. Lenses weaker than 0.75 D. were not prescribed for patients with permanent squint. The glasses were worn for at least four months prior to operation. When the child obtained the age of 8 years, the correction was adjusted according to the value stated by Donders.

Occlusion of the good eye only was performed from the age of 1-1½ years, and this treatment was continued for one to four days a week. This was done even after surgery had produced binocular fixation if the visual acuity of the squinting eye, when measurable, proved to be reduced.

All the operations were carried out under tribromoethanol (Avertin) anesthesia. Experience with this form of anesthesia has been published (Nordlöw [16]). The following surgical procedures were employed: tenotomy controlled with sutures on one side in cases of static angle of squint of approximately 10 degrees; simultaneous tenotomy controlled with sutures of the medial rectus and resection and advancement of the lateral rectus on the same eye in cases of squint of 15 degrees and over. The operative procedure was, in principle, the same as that described by Nordlöw.[12]

7. *Statistical Analysis.*—Current formulae and methods were employed.

REVIEW OF THE MATERIAL

The material comprises (1) 70 cases of permanent convergent squint from the eye department of the Central Hospital in Vänersborg, in which opera-

§ References 11, 12, and 14.

tion was performed early, and (2) 96 cases of permanent convergent squint from the eye outpatient department of the Seraphim Hospital, Stockholm, collected at random and followed up. The latter material is included as a control material. All cases were examined and treated by me.

1. *Cases of Permanent Convergent Squint Operated on Early.*—With one exception, early operation was proposed in all cases of permanent convergent squint brought for treatment in which the squint had developed at the age of 6 months or later but had not been present for more than four years. The cases in which the visual acuity could not be improved to more than 2/60, and in which there was no definite central fixation, were excluded. These comprise 5.9±1.64% of the total number. An additional 14.6±2.47% were excluded, that is, cases in which operation was refused. The patients constituting this group did not differ from those operated on, and so their exclusion does not influence the composition of the material in any specific way. The group of 5.9% differs from the group of patients operated upon in that central fixation was absent. In a number of cases the poor visual acuity may have been due to unsatisfactory occlusion for amblyopia. The prognosis in these cases, when they are well cared for, should not differ from that in the cases operated on. A number of cases in the group may have a poorer prognosis. If they are excluded, the group of cases operated on may present a more favorable composition than a representative material. Where this factor may be of significance in the results, the calculations will be made with the exclusion or the inclusion of this group of 5.9%.

Of the cases of convergent squint operated upon early, which represent two-thirds of all cases of permanent convergent squint (Nordlöw [15]), 70 have now attained the age of 9 to 17 years. This group, which will be the subject of analysis, comprises all cases which satisfy the requirement of age; 32 boys and 38 girls are concerned. To determine whether these cases constitute a representative sample of the group of cases of permanent convergent squint from which they were selected, the age distribution at the time of development of the squint will be examined (Table 1). This will be compared with the age distribution in a total material, published previously (Nordlöw,[15] Table 7).

TABLE 1.—*Age Distribution at Development of Squint in 270 Cases (Group I) of Permanent Convergent Squint Collected at Random and Examined Within Three Years of Development of Squint* and 70 Cases (Group II) of Permanent Convergent Squint Operated upon Early and Followed Up for a Prolonged Period*

Group	No. of Cases	Age at Development of Squint, Yr.							
		0-0.5	0.5-1	1-2	2-3	3-4	4-5	5-6	6-7
I	270	98	45	37	30	17	9	3	2
II	70	—	11	23	14	13	6	2	1

* Nordlöw,[15] Table 7

TABLE 2.—*Distribution of Primary Static Angle of Squint at Five Meters in Seventy Cases of Permanent Convergent Squint Operated upon Early*

No. of Cases	Magnitude of Angle of Squint, Degrees								
	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50
70	12	18	10	8	12	7	2	—	1

TABLE 3.—*Interval from Development of Squint Until First Operation in Seventy Cases of Permanent Convergent Squint Operated upon Early*

No. of Cases	Interval, Yr.							
	0-0.5	0.5-1	1-1.5	1.5-2	2-2.5	2.5-3	3-3.5	3.5-4
70	1	14	15	4	15	3	7	11

It appears from Table 1 that the group 0.5-1 year of age is underrepresented and the group of 3-4 years is overrepresented in the material of cases operated upon. A statistical analysis shows that in no year group do the differences amount to twice their standard error. The agreement between the two materials as regards age at the time of development of the squint must, therefore, be considered to be good.

Where the material operated upon is concerned, an account will also be given of the distribution of the primary static angle of squint at 5 meters (Table 2), the interval between the development of squint and the first operation (Table 3), the interval between the development of squint and the operation which first rendered binocular fixation (Table 4), the number of operations carried out (Table 5), and the age distribution at the final examination (Table 6). Other conditions will be taken into account, together with the results.

The static angle of squint for 5 meters in 35 cases was between 5 and 18 degrees, and in 35 cases, between 18 and 50 degrees. Table 3 shows that half the cases were operated upon from one to two and one-half years after the development of the squint and that approximately one-fourth were operated on earlier and one-fourth later than that. In a number of cases operated upon twice or thrice the establishment of binocular fixation was even longer delayed (Table 4).

The number of operations and cases with binocular fixation are noted in Table 5. Where later

TABLE 4.—*Interval from Development of Squint Until the Operation Which First Rendered Binocular Fixation in Fifty-Four Cases of Permanent Convergent Squint Operated upon Early*

No. of Cases	Interval, Yr.										
	0-0.5	0.5-1	1-1.5	1.5-2	2-2.5	2.5-3	3-3.5	3.5-4	4-4.5	4.5-5	5-5.5
54	1	7	12	3	9	3	10	3	3	2	1

changes in the mutual position of the eyes were not concerned, the second and third operations were carried out one to seven months after the preceding operation; in the majority of cases after two to four months.

Out of the 70 cases, constituting the total number of cases of permanent convergent squint in which operation was performed and which had attained the age of 9 to 17 years at the final examination, 64 could be followed up during the entire period. The age distribution of these cases at the final examination appears in Table 6. Of the six cases which could not be followed up, two did not reappear and four had moved to remote places. When they were last examined, binocular fixation was present in three after one to two operations and was absent in three after one operation. There is no reason to suppose that the exclusion of these cases influences the remaining material in any particular way.

2. Control Material.—This was treated in the same way as the preceding material but was not operated upon. This material was previously described in detail (Nordlöw,[14] 1951). It comprises 96 cases, viz., 36 boys and 60 girls, suffering from permanent convergent squint. The average age at the first examination was 5.1 years, and that at the last examination, 15.3 years. The material was followed up on an average for 10.2 years, with an average of 7.9 follow-up examinations, or somewhat less than one examination a year.

During the period of observation, the primary static angle of squint remained unchanged in 45.8±5.09%, increased (5-22°) in 12.5%, and decreased (3-24°) in 41.7%. If the upper limit for the angle of squint is set at ±6° or ±8°, 11.5% and 14.6% recovered cosmetically. Functional recovery was obtained in one case (1%) with binocular fixation, stereoscopic vision, amplitude of fusion, and normal retinal correspondence. If this case is included, only 6.7% had normal retinal correspondence left at the final examination. The visual acuity at the final examination was less than 0.3 in 29.2%. In half these cases central fixation was absent.

TABLE 5.—*Distribution of Number of Operations and Cases with Binocular Fixation in Seventy Cases of Permanent Convergent Squint Operated upon Early*

No. of Operations	No. of Cases	No. of Cases with Binocular Fixation
1	70	38
2	19	14
3	3	2

TABLE 6.—*Age Distribution at Final Examination in Sixty-Four Cases of Permanent Convergent Squint Operated upon Early and Followed Up for a Prolonged Period*

No. of Cases	Age, Yr.							
	9-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17
64	19	11	13	13	1	3	3	2

RESULTS

The experience gained concerning the cases of permanent convergent squint operated upon early will be discussed in this section according to the following criteria: (1) presence or absence of binocular fixation in connection with the operations, (2) changes in this quality during the period of observation, and (3) condition at the final examination. An evaluation of the method employed in determining the visual acuity in infants prior to operation and the binocular vision after operation will be included in the account.

1. The material comprises 70 cases. At the first operation, tenotomy controlled with sutures was carried out in 25 cases, while simultaneous tenotomy controlled with sutures of the medial rectus and muscle resection-advancement of the lateral rectus of the same eye was carried out in 45 cases. Binocular fixation could be demonstrated one week to four months after the intervention in 38 cases. In the remaining 32 cases, residual esotropia of 2°-15° persisted in 27 cases, divergent squint of 2°-10° in 4 cases, and only vertical deviation in 1 case. In 19 of these 32 cases a second operation was

done: Tenotomy controlled with sutures was employed in 17 cases and advancement in 2 cases. Thereby binocular fixation was obtained in an additional 14 cases (Table 5), i. e., in 52 cases binocular fixation was obtained after one to two operations. The reasons why a second operation was not performed in 13 cases are recorded in Table 7.

Of the five cases in which binocular fixation was not obtained after two operations, three underwent a third operation, viz., advancement of tenotomized muscle. Following this intervention, binocular fixation was obtained in two cases. The reason why two patients were not operated upon was slight

TABLE 7.—*Reasons Preventing a Second Surgical Intervention in Thirteen Cases of Permanent Convergent Squint Operated upon Early*

Reason	No. of Cases	Angle of Squint, Degrees	
		Convergent 5-10	Divergent 2-10
Medical indications	1	1	..
Operation refused	2	2	..
Patient did not reappear	1	1	..
Instructions not followed	2	1	1
Removed	2	2	..
Angle of squint too small	5	4	1
Total	13	11	2

angle of squint in the one case, and the desire to avoid renewed intervention in the other. In the present material, no intervention with the object of correcting possible vertical deviation was performed.

From the data above it is apparent that 54 cases, or 77.1±5.0%, acquired binocular fixation following one to three operations. Of the 16 cases which did not acquire binocular fixation, 13 were operated upon once only. Out of these, 7 (Table 7) may have undergone one or two additional operations. If the treatment could have been carried through, the number of cases with binocular fixation would probably have increased in this material. As compared with a similar material reported by Nordlöw,[13] in which 91±6.1% acquired binocular fixation, the difference becomes 13.9±7.9%, i. e., less than twice the standard error. This good agreement becomes more apparent in considering the data above. If the original 70 cases are supplemented by 5.9% which were excluded on account of absence of central fixation, the percentage of cases which obtained binocular fixation becomes 73.0±5.16%. In the present representative material, the incidence of binocular fixation lies primarily between 73.0% and 77.1%.

2. The material comprises 64 cases, 51 of which had binocular fixation originally after surgery and 13 of which still squint. With regard to changes occurring spontaneously during the period of observation, these two groups will be analyzed individually.

In 36 of the group of 51 cases with binocular fixation, this condition remained unchanged during the entire period of observation. In 15 patients, however, or in 29.4±6.38%, squinting appeared. In seven cases convergent squint was concerned. The relapse took place at the age of 6 to 13 years, after binocular fixation had been present for one to seven years. In eight cases the squint was divergent. It occurred at the age of 5-9 years, after binocular fixation had been present for 0.5 to 6 years. Of the seven cases in which convergent squint appeared, five had previously showed orthophoria, and two, esophoria of up to 5 degrees. Of the eight cases in which divergent squint occurred, six had previously shown orthophoria, one esophoria, and one exophoria. Of the 15 cases in which squint reappeared, 8 were operated upon once again, and binocular fixation was thereby obtained again in 7 cases. More detailed information regarding these interesting cases is compiled in Table 8.

Changes also appeared in the group of 13 cases in which binocular fixation was not obtained in connection with early operations. In six of these cases the angle of squint diminished and binocular fixation occurred (Table 9). The determination of whether the angle of squint had diminished was not based on comparison of two single measurements; several observations were carried out prior to and after the occurrence of binocular fixation. In the remaining seven cases the angle of squint persisted unchanged: convergent 5°-10° in five cases, convergent

TABLE 8.—*Information Concerning Fifteen Cases of Permanent Convergent Squint with Binocular Fixation Operated upon Early in Which Squinting Recurred*

No.	Interval from Development of Squint Until Operation Rendering Binocular Fixation, Yr.	No. of Operations	Age at Final Operation, Yr.	Position of Eyes Following Final Operation, "Cover Test" Method	Age at Development of Spontaneous Change, Yr.	Convergent Squint in Perimeter, Degrees	Divergent Squint in Perimeter, Degrees	Age at Reoperation, Yr.	Age at Final Examination, Yr.	Binocular Fixation	Stereoscopic Vision	Ability of Fusion	Retinal Correspondence
1	1 1/12	1	2 3/12	Orthophoria	5	10	5	7 2/12	12 11/12	Yes	Good	Good	n
2	1 1/12	1	2 1/12	Same	5	10	..	10 4/12	17 9/12	Intermit.	Good	Good	n an
4	3 4/12	1	6 4/12	Same	12 4/12	11	..	12 7/12	15 6/12	Yes	Good	Good	n
6	1 1/12	2	2 1/12	Same	8 1/12	..	15	.....	11 1/12	No	.....	.....	n
8	1 1/12	2	2 10/12	Same	5 10/12	..	5	.....	11 7/12	No	.....	.....	an
9	7/12	1	5	Same	7	Yes	5	7 6/12	14 8/12	Yes	Good	Good	n
22	3 4/12	2	4 10/12	Same	6 10/12	..	5	.....	12 1/12	No	.....	.....	an
32	1 5/12	2	3 8/12	Esophoria, 5°	6 8/12	10	5	9	10 1/12	Yes	Good	Good	n
40	3 10/12	1	5 4/12	Orthophoria	5 10/12	..	5	.....	12 5/12	No	.....	.....	an
41	2 4/12	2	2 8/12	Same	9 6/12	..	..	.....	9 6/12	No	.....	.....	..
44	2	1	3	Same	6	4	..	.....	9 5/12	Yes	.....	.....	Exc.
56	8/12	1	5 5/12	Same	9	..	5	10 1/12	10 4/12	Yes	Good	Good	..
59	3	1	5	Exophoria	6 6/12	..	9	7 3/12	10 5/12	Yes	Good	Good	n
60	1 5/12	2	4 5/12	Esophoria, 5°	5 5/12	10	..	6 1/12	10 9/12	Yes	Good	Good	an
64	1 5/12	1	5 2/12	Esophoria, 2°	.....	..	7	.....	9 11/12	Yes	Good	.....	n

n = normal; an = anomalous.

10°-15° in one case, and divergent 10° in one case. Despite the occurrence of these changes, binocular fixation was preserved at the termination of the period of observation in 37+7+6, or 50 cases, viz., 78.1±5.17%, or 73.5±5.35% if 5.9% without central fixation are included.

Of the 51 cases in which binocular fixation was obtained primarily, 36, or 70.6±6.38%, remained unchanged. On comparison with the control material, in which the angle of squint remained unchanged in 45.8±5.09%, the difference becomes 24.8±8.16% in favor of the material operated upon. The difference is thrice the standard error and is significant. This indicates that binocular fixation established early counteracts later spontaneous changes in the relative position of the eyes in patients with permanent convergent squint.

3. The material comprises 64 cases. Concerning the final examination, an account is given for age distribution (Table 6), the interval from the occasion of the first and the last binocular fixation to the final examination, the position of equilibrium of the eyes, stereoscopic vision, amplitude of fusion, retinal correspondence, and visual acuity.

The average age at the final examination was 11⅓ years, with the limits of 9 and 17 years. It is also of interest to know for how long binocular fixation had been present in the 50 cases which possessed this ability at the final examination. As changes occurred and new surgical interventions were undertaken during the period of observation, the duration of binocular fixation was calculated partly from the first occasion on which binocular fixation could be observed (Group I) and partly from the last occasion (Group II). The time distribution is tabulated in Table 10. The average duration for Group I is 6$\frac{2}{12}$ years, with the limits of 1 to 11 years. The actual duration of binocular fixation is somewhat shorter, although not so short as for Group II.

In the group of 50 cases with binocular fixation, 43 were examined with Herschel's double prism after correction of errors of refraction. The results at 5 meters were

TABLE 9.—*Information Concerning Six Cases of Permanent Convergent Squint Operated upon Early Without Binocular Fixation in Which This Ability Developed Spontaneously Later*

Case No.	Interval from Development of Squint Until Final Operation, Yr.	No. of Operations	Age at Final Operation, Yr.	Position of Eyes Following Final Operation, "Cover Test" Method	Age at Spontaneous Development of Binocular Fixation, Yr.	Age at Final Examination, Yr.	Binocular Fixation	Stereoscopic Vision	Ability of Fusion	Retinal Correspondence
17	2	1	4	Conv. 7°	11	12 5/12	Yes	Good	Good	n
19	2	1	7	Conv. 2°	9	14 7/12	Yes	Good	Good	n
21	4	1	8	Conv. 5°	.....	16 9/12	Yes	Grade I	Good	n
28	1 7/12	1	2 7/12	Div. 10°-15°	5 7/12	16 2/12	Yes	Grade I	.....	n
37	3	1	3 10/12	Conv. 8°	5 4/12	10 9/12	Yes	.....	.....	..
55	1 2/12	1	4 10/12	Conv. 5°	.....	10 4/12	Intermitt.	.....	.....	..

TABLE 10.—*Distribution of Periods of Observation from First (I) to Final (II) Occasion in Which Binocular Fixation Could Be Observed in Fifty Cases of Permanent Convergent Squint Operated upon Early*

		Time, Yr.									
No.	Group	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11
50	I	1	5	4	5	8	10	4	5	5	3
50	II	3	5	7	7	6	9	5	3	4	1

as follows: orthophoria in 15 cases; esoexophoria, 1°-3° in 17 cases, 3°-5° in 6 cases, 5°-7° in 4 cases, and 7°-9° in 1 case, and in 7 cases a combination with hypophoria or hyperphoria of 1°-2°. Heterophoria at 0.5 meter is of interest partly in determining whether a pathological connection exists between convergence and accommodation and partly as a comparison with the estimated value for 0.5 meter. Measurement at 0.5 meter was, unfortunately, available in 22 cases only. The standard error of a single determination is ±0.59°, and when two single values are compared

$$\pm\sqrt{0.59^2+0.59^2}=\pm 0.83^\circ.$$

The limits of the random error of the comparison thus become ±2.5°. Two determinations completely independent of one another are, however, not included in the comparison in question. Instead, they were carried out during one and the same session, for which reason the limits of the real value should be less than ±2.5°, but greater than ±1.8°. The value of ±2° has therefore been employed in the present calculation. From Table 11 it appears that the 13+2+5=20 cases fall within these limits. Thus, in these cases the values for heterophoria measured 5 meters and at 0.5 meter should be identical. In two cases the esophoria at 0.5 meter was 1°-2° greater than at 5 meters.

In Table 12, the estimated and the measured values for heterophoria at 0.5 meter in each individual case are compared. Here, the standard error of the comparison is composed of the standard error of the determination and the standard error of the estimation. The limits of the random error of the comparison should exceed ±2.5° and were assumed to be ±3.0°. Assuming this, 20 cases lie within these limits, and 2 cases, 1° outside in favor of the value determined. The values are in good agreement.

The position of equilibrium of the eyes after correction of errors of refraction, and measured on the synoptophore, was compared with the value obtained with Herschel's prism at 5 meters in each individual case.

TABLE 11.—*Comparison of Values Obtained with Herschel's Prism at 5 Meters and 0.5 Meter with Complete Correction of Errors of Refraction in Twenty-Two Cases of Permanent Convergent Squint Operated upon Early*

Heterophoria in Horizontal Plane	No. of Cases	Excess Heterophoria at 5 M. Over 0.5 M., Degrees			Excess Heterophoria at 0.5 M. Over 5 M., Degrees	
		3-5	1-3	0	1-3	3-5
Esophoria	16	..	2	9	4	1
Exophoria	6	..	..	4	2	..

Limits of the real value ±2°

TABLE 12.—*Comparison of Estimated and Measured Values for Heterophoria in Horizontal Plane at 0.5 Meter in Twenty-Two Cases of Permanent Convergent Squint Operated upon Early*

Heterophoria	No. of Cases	Excess Estimated Value, Degrees			Excess Measured Value, Degrees	
		3-5	1-3	0	1-3	3-5
Esophoria	16	..	1	7	5	3
Exophoria	6	..	1	..	2	3

Limits of the real value ±3°

correct locating of at least two of the squares in the picture for testing stereoscopic vision — Grade 2, and correct location of all four squares — Grade 3. For evaluation of stereoscopic vision, measurements in 48 out of the 50 cases are available. In 46 cases, the stereoscopic vision was of Grade 3; in 1 case, of Grade 2, and in 1 case, of Grade 1. In Table 14 the stereoscopic vision was correlated with the grade of heterophoria, presence of amplitude of fusion, and retinal correspondence.

TABLE 13.—*Comparison of Values Obtained with Synoptophore and Herschel's Prism at 5 Meters and with Complete Correction of Errors of Refraction in Forty-Three Cases of Permanent Convergent Squint Operated upon Early*

No. of Cases	Direction of Heterophoria	Excess Value with Herschel's Prism, Degrees				Excess Value with Synoptophore, Degrees		
		3	2	1	0	1	2	3
43	Horizontal.....	1	6	4	13	6	10	8
43	Vertical.....	..	2	1	36	5	1	..

Limits of the real value ±2.5°

TABLE 14.—*Interrelationship at Final Examination of the Position of Equilibrium, Stereoscopic Vision, Amplitude of Fusion, and Retinal Correspondence in Forty-Eight Cases of Permanent Convergent Squint Now Possessing Binocular Fixation*

No. of Cases	Position of Eyes in Synoptophore	Degree of Stereoscopic Vision			Presence of Amplitude of Fusion		Retinal Correspondence*		
		1	2	3	Yes	No	n	n + an	an
16	Orthophoria	..	1	14	14	..	13	..	3
12	Eso-exophoria 1-3°	..	..	12	11	1	9	1	..
12	Same 3-5°	..	..	12	11	1	11	..	..
5	Same 5-7°	..	..	5	3	2	4	1	..
3	Same 7-9°	..	..	3	2	1	3	..	..
48		..	1	46	41	5	40	2	3

* Here, n = normal; an, anomalous.

If the standard errors for the synoptophore and for Herschel's prism are assumed to be identical, the limits of the random error of the comparison become ±2.5°. It appears from Table 13 that 2 out of the 43 cases fall 0.5° outside these limits. The results with the two methods are in good agreement.

Starting from the position of equilibrium of the eyes in the synoptophore ("Methods," Point 5*b*), stereoscopic vision and amplitude of fusion in the horizontal plane were determined. Stereoscopic vision was graded in the following way: Fusion of simple figures with certain common parts — Grade 1;

For judgment of the amplitude of fusion, values of measurements or attempted measurements in 46 out of the 50 cases are available (Table 14). In 5 out of the 46 cases the amplitude of fusion could not be measured on account of suppression of the image from the one eye. The amplitude of fusion was assumed to be 0 (degrees) in these cases. In the following calculations, these cases have not been included among those in which amplitude of fusion could be measured.

Two measurements of amplitude of fusion were carried out in all directions. The average difference for the first and the second series of measurements in all directions is

less than once the standard error. Both series can therefore be considered to belong to the same curve of distribution. The mean of the two values measured in the various directions could therefore be employed for each case in the following calculations for 41 cases:

Amplitude of Fusion from the Position of Equilibrium Outward: M—5.1°±0.28°; σ—±1.79°. Normal value: M—5.0°±0.13°.

The difference of 0.1° in favor of the material operated upon is less than once the standard error. In the material operated upon, the average amplitude of fusion in this direction must therefore be regarded as normal.

Amplitude of Fusion Toward the Position of Equilibrium Inward: M—2.4°±0.23°; σ—±1.48°. Normal value: M—1.6°±0.11°.

The difference, 0.8°±0.25°, in favor of the material operated upon is greater than thrice the standard error and is significant. In the material operated upon, the amplitude of fusion in this direction is greater than normal.

Amplitude of Fusion from the Position of Equilibrium Inward Without Accommodation: M—4.6°±0.42°; σ—±2.67°. Normal value: M—6.7°±0.28°.

The difference, —2.1°±0.50°, in favor of normal cases is greater than thrice the standard error and is significant. In the material operated upon, the amplitude of fusion in this direction is less than normal.

Amplitude of Fusion from the Position of Equilibrium Inward with Accommodation: (24 cases): M—12.4°±1.60°; σ—±7.84°. Normal value: M—16.7°±0.83°.

The difference, —4.3°±1.80°, in favor of normal cases is greater than twice, but less than two and a half times, the standard error, for which reason agreement may be considered satisfactory. In this material, the amplitude of fusion is normal; in a larger material it may turn out to be reduced.

Amplitude of Fusion Out Toward the Position of Equilibrium: M—2.0°±0.26°; σ—±1.67°. Normal value: M—3.9°±0.33°.

The difference, —1.9°±0.42°, in favor of normal cases is greater than thrice the standard error and is significant. In the material operated upon, the amplitude of fusion in this direction is less than normal.

The investigation revealed that amplitude of fusion was absent in 5 cases and present in at least 41 cases, viz., 64.1%±6.0% of the total number of cases observed (64), or 60.3%±5.93% if 5.9 cases in which central fixation was absent are included. The correct value should be between 60.3% and 64.1%. The amplitude of fusion in these cases proved to be normal or greater than normal lateral to the position of equilibrium and less than normal medial to the position of equilibrium. The explanation of this may be that in commencing convergent squint and in esophoria (see "Material," Point 3) the amplitude of fusion is practiced less medial to than lateral to the position of equilibrium.

Retinal correspondence could be measured in 45 cases, while in 2 cases it could not be measured on account of suppression of the image from the one eye. Concerning three cases, results of measurements are not available. At the final examination, retinal correspondence was normal in 40 cases, alternately normal and anomalous in 2 cases, and anomalous in 3 cases (Table 14). It was investigated once in 21 cases, twice in 20 cases, thrice in 3 cases, and four times in 1 case, at intervals of approximately one year (Table 15). In 80.0%±5.7% of those cases which possessed the ability of binocular fixation, evidence of normal retinal correspondence was found at the final examination. In a number of the remaining 20%, simultaneous normal and anomalous projection was probably present. The fact that five cases possessed stereoscopic vision is evidence of this (Table 14). The four examinations with normal and anomalous retinal correspondence in Table 15 refer to four cases in which the second of the two examinations showed normal retinal correspondence.

Consideration of the results of the examination as regards the distribution of binocular vision in the entire material of 64 and 68 cases, respectively, when 5.9% without cen-

TABLE 15.—*Distribution of Normal, Normal and Anomalous, and Anomalous Retinal Correspondence in the Various Investigations in Forty-Five Cases*

No. of Examinations per Case	No. of Cases	Retinal Correspondence per Examination*		
		n	n + an	an
1	21	19	..	2
2	20	34	4	2
3	3	9	..	..
4	1	4	..	..

* Here, n indicates normal; an, anomalous.

tral fixation are included in the latter figure reveals the following facts: Binocular fixation are obtained in 78.1%±5.17% and 73.5%±5.35%, respectively; functional cure, orthophoria or slight heterophoria, stereoscopic vision, amplitude of fusion, and normal retinal correspondence (38 cases) were present in 59.4%±6.13% and 55%±6.02%, respectively. More or less defective binocular vision was present in 15.6% and 14.7%, respectively. When cases which began to squint during the first six months of life are excluded, the control material contains 1 case functionally cured out of 66 cases, or 1.5%±1.50%. Compared with the frequency of functional cure in the material operated upon, the difference becomes 57.9%±6.31% and 53.5%±6.06%, respectively, i. e., thrice the standard error and is significant. The difference is very considerable and in favor of the material operated upon.

Under "Methods," Point 5*a*, "binocular fixation" at 0.5 meter was described and stated as the method employed in this paper for determination of the presence of binocular vision in preschool and older children. This method was employed as a control for the result of operation in early surgical intervention in convergent squint. It may be employed as soon as the child can fixate a point of light. By following up the children until they are older and exact measurements of binocular vision can be undertaken, an impression of the value of the method may be obtained. Of 50 cases with binocular fixation, 48 could be investigated in detail. Of these, all cases possessed binocular single vision; 47 cases, stereoscopic vision; 1 case, fusion of simple figures; 41 cases, amplitude of fusion, and 40 cases, normal retinal correspondence. In all cases in which the method proved binocular fixation to be absent, squinting was revealed on further investigation. The method "binocular fixation," under the given conditions, may therefore be recommended for control of the presence of binocular vision and employed, *inter alia*, in early operation of squint.

The final visual acuity corrected with glasses in the 64 cases of permanent esotropia operated upon early is recorded in Table 16. In no case does the squinting eye lack central fixation. In five cases the visual acuity is less than 0.3. If the excluded 5.9%, or four cases which lacked central fixation from the beginning, are included, the result becomes 9 cases, or 13.2%, with visual acuity of less than 0.3. This appears to be, and may be, a better result than the 29.2% in the control material. It must, however, be remembered that this material also includes the cases which had squinted since the first months of life. The possibility that the visual acuity in these cases tends to be poorer cannot be entirely excluded. In the material operated upon no eye showed changes in the media or the fundus. To evaluate correctly the visual acuity obtained, several additional factors should be taken into consideration, but this would involve too extensive a subdivision of the material.

TABLE 16.—*Final Visual Acuity with Correction by Glasses in Sixty-Four Cases of Permanent Convergent Squint Operated upon Early*

Position of Eyes	No. of Cases	Eye	Visual Acuity									
			0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
Binocular Fixation	50	Good	—	—	—	—	—	—	—	—	1	49
		Bad	1	1	4	12	6	6	4	3	2	11
Squinting	14	Good	—	—	—	—	—	—	—	1	1	11
		Bad	—	3	2	1	3	—	1	—	1	3

It appears, further, from Table 16 that 59 out of 64 squinting eyes acquired at least a visual acuity of an order which rendered reading possible. This demonstrates that the method employed (Point 1) of registering the way in which infants prior to the age of 3 to 4 years fixate a point of light renders a satisfactory final result regarding visual acuity.

There remain to be examined the results from the final examination of 14 cases which were still squinting. In eight cases convergent squint of 5°-15° and in six cases divergent squint of 5°-18° was present. If an angle of squint of approximately 5 degrees is regarded as cosmetically satisfactory, 10 cases, or 15.6% of the entire material, satisfies this requirement.

The question arises why these cases had not acquired binocular fixation. It should be recalled that seven cases had never been entirely relieved from the static angle of squint surgically. Binocular vision has therefore never had the opportunity of functioning and developing in these cases. In seven cases binocular fixation was present for a shorter or longer period. Defects in binocular vision, perhaps pronounced suppression or poor amplitude of fusion, were presumably present, anyhow at the time of operation, and caused the unsuccessful results in these cases.

The quality of stereoscopic vision or amplitude of fusion was not tested. The retinal correspondence was examined in nine cases. The result obtained was normal in one case; normal and anomalous, in one case; suppression of the image from the one eye, in one case, and anomalous, in six cases. The first two cases possessed binocular fixation for a period. The frequency of normal retinal correspondence is in agreement with that found in the control material at the age of 13 to 14 years, viz., 9%. The results obtained as regards visual acuity have already been discussed and are recorded in Table 16.

COMMENT

Some views concerning the treatment and the mechanism of development of esotropia are now presented. The material treated surgically is representative of cases of permanent convergent squint in which squinting commenced at the age of 6 months or later. This group comprises two-thirds of all cases of permanent convergent squint, and the conclusions concern this group.

Under the experimental conditions stated, 73.5% to 78.1% of the material operated upon early had binocular vision at an average age of 11⅓ years (limits 9 and 17 years). Of the material, 55%-59.4% had functional cure, with orthophoria or heterophoria compensated by fusion, stereoscopic vision, amplitude of fusion, normal retinal correspondence, and at least reading vision (0.3) in the squinting eye. In addition, 14.7%-15.6% had binocular fixation with more or less defective binocular vision. A further 15.6% were cosmetically cured. Still earlier surgical treatment might have rendered even better results.

In a control material treated conservatively, with neither orthoptic training nor early operation, 1.5% were functionally cured and 11.5%-14.6% were cosmetically cured. The figures recorded demonstrate significantly the superior results of early operation. To estimate the value of orthoptic training, a material representative of and similar to the present one must be established. This should be treated with both orthoptic training and early operation. At present, "suitable" cases are selected for orthoptic training, so that the material does not become representative. Douglas[3] (1952), who is well aware of these problems and assumes a healthy critical attitude, cannot definitely ascertain the value of orthoptic training in his own material.

The decisive significance of the mechanical factors for the development of permanent and, in a great number of cases, of intermittent esotropia was previously demonstrated in a more indirect way by Nordlöw.¶ An investigation on man may now be conceived in which only the position of the eyes in the muscle ring is altered by surgery, as soon as possible after development of the

¶ Reference 11, pp. 76-78.

squint. Apart from the altered position of the eyes, the other conditions should be the same prior to and after operation. If it is possible to obtain lasting binocular fixation and normal binocular vision in this way, the significance of the mechanical factors would be demonstrated in an direct manner. The result recorded in this paper arises from an experimental investigation on squinting children conducted in this way. On account of the difficulties of controlling a clinical material, the occasion for operation had to be extended up to four years after the development of the squint. A mechanical factor could be demonstrated as a cause of the development of esotropia in the 55%-59.4% of the cases which were cured functionally. This is also probable in a further 14.7%-15.6% with binocular fixation but with defects in binocular vision. It is further possible in these cases of the material in which operation was not entirely successful in eliminating the squinting position.

SUMMARY

A series of cases of permanent esotropia in which squinting commenced at the age of 6 months or later, thus representing two-thirds of all cases of permanent esotropia, were operated upon 0.5-4 years after the development of the squint. The material comprises 70 cases. After one to three operations, 73%-77.1% obtained binocular fixation.

Of the material, 64 cases could be followed up until an average age of 11⅓ years, the limits being 9 to 17 years. During the period of observation, 29.4% of the cases with binocular fixation lost this function, and some of them were operated upon again. Of the cases which still squinted, approximately half obtained spontaneous binocular fixation. At the conclusion of the period of observation, 73.5%-78.1% possessed binocular fixation.

Of the cases with binocular fixation, one-third had orthophoria and two-thirds heterophoria at the final examination; 55%-59.4% were cured, with good binocular vision; 14.7%-15.6% had defects in binocular vision, and 15.6% had cosmetic cure only. Among 64 cases, the visual acuity of the squinting eye was less than 0.3 in 5 eyes and greater than this in the remainder. The result is significantly better than in a control material not operated upon but otherwise treated in the same manner.

The method of determining the visual acuity prior to operation in a child below the age of 3 to 4 years by observing his manner of fixating a point of light and of determining the presence of binocular vision after operation with "binocular fixation" has rendered satisfactory result. The method may therefore be recommended.

An investigation of the mechanism of development of esotropia in the light of the results obtained has revealed a mechanical factor as the only tangible cause in at least 70% of the cases, and probably more.

Kungsgatan 1B.

REFERENCES

1. Bettremieux: Prognostic de curabilité du strabisme, Arch. opht. **44**:442, 1927.

2. Dahlberg, G., and Nordlöw, W.: Genetics of Convergent Strabismus, Acta genet. et statist. med. **2**:1, 1951.

3. Douglas, A. A.: Value of Orthoptics in the Treatment of Squint, Brit. J. Ophth. **36**:169, 1952.

4. Dunnington, J. H.: The Proper Time for Operation in Strabismus, Arch. Ophth. **10**:438, 1933.

5. Exnerovâ, M.: Result of Operative Treatment of Squint in Children, Českoslov. oftal. **4**: 383, 1948; Excerpta Med. XII **3**:409, 1949.

6. Forsmark, E.: Surgical Treatment of Squint, Hygiea **94**:922, 1932.

7. Hepburn, M.: Symposium on Nonparalytic Squint, Tr. Ophth. Soc. U. Kingdom **52**:366, 1932.

8. Huggert, A.: Early Operation in Squint: Some Results, Acta ophth. **32**:700, 1954.

9. Lowell, J. W.: Surgical Treatment of Squint, Am. J. Ophth. **9**:600, 1926.

10. Mügge, F.: Zur operativen Behandlung des Einwärtsschielens, Klin. Monatsbl. Augenh. **105**: 190, 1940.

11. Nordlöw, W.: Über den Entstehungsmechanismus des Einwärtsschielens, Göteborg, Elanders Boktryckeri Aktiebolag, 1942, p. 134.

12. Nordlöw, W.: Über den Entstehungsmechanismus und die Frühoperation des permanenten Einwärtsschielens, Acta ophth. **23**:97, 1945.

13. Nordlöw, W.: Accuracy of the Objective and Subjective Method of Determining the Refraction of the Eye, Acta ophth. **27**:349, 1949.

14. Nordlöw, W.: Spontaneous Changes in Refraction and Angle of Squint Together with the State of Retinal Correspondence and Visual Acuity in Concomitant Convergent Strabismus During the Years of Growth, Acta ophth. **29**:383, 1951.

15. Nordlöw, W.: Age Distribution of the Onset of Esotropia, Brit. J. Ophth. **37**:593, 1953.

16. Nordlöw, W.: Tribromethanol Anesthesia in Eye Surgery, Acta ophth. **31**:127, 1953.

17. Peter, L. C.: Symposium on the Treatment of Non-Paralytic Squint, Tr. Ophth. Soc. U. Kingdom **52**:325, 1932.

18. Pollock, W. B. J.: Squint: The Question of Early Operation, Lancet **1**:1296, 1921.

19. Pollock, W. B. J.: The Advisability of Early Operation in Strabismus Convergens, Brit. M. J. **2**:733, 1921.

20. Riise, P.: Results in Binocular Vision by Early Operation in Esotropia, Acta ophth. **31**:117, 1953.

21. Rønne, G.: The Basic Principles in Squint Treatment with Special Reference to the Physiology and Pathophysiology of Binocular Vision, Acta ophth. **32**:681, 1954.

22. Rønne, H.: Indications and Proper Time for Operating in Squint in Light of the Pathogenesis of Secondary Squint, Hospitalstid. **3**:1225; 1249, 1910.

23. Smith, P.: On the Treatment of Strabismus in Young Children, Proceedings IX International Congress of Ophthalmology, 1899.

24. Stanworth, A.: Final Results of Squint Operations in Which Restoration of Binocular Single Vision Was Not Expected, Brit. J. Ophth. **33**:477, 1949.

25. Wiesinger: Neuere Methoden der Schielbehandlung, Berl. klin. Wchnsch. **43**:1025, 1906.

Mechanism of Serous Choroidal Detachment

A Review and Experimental Study

STANLEY A. CAPPER, M.D., M.Sc.
and
IRVING H. LEOPOLD, M.D., D.Sc., Philadelphia

Although a number of articles have been written on the subject of serous choroidal detachment, most of these have been case reports, with conclusions that were both speculative and indecisive. The frequency with which this entity occurs as a complication of intraocular surgery makes it imperative that the subject be investigated more thoroughly as to cause and methods of prophylaxis. Fortunately, most serous choroidal detachments resolve completely without specific therapy; nevertheless, they always cause much anxiety on the part of the attending ophthalmologist, as well as the patient. A few investigators (Fronimopoulos,[9] Meesmann [14]) have done basic research on this problem. The present work was undertaken to study serous choroidal detachment as to its etiology and mechanism of production.

HISTORICAL SURVEY

Knapp (1868) was the first to report serous choroidal detachment following cataract extraction. He proposed the theory that fluid accumulated as a result of plastic scleritis. There were only 10 additional cases reported prior to 1900.

Fuchs * (1900) found many cases of serous choroidal detachment following both glaucoma and cataract operations. He felt that when the anterior chamber was opened there was a tear of the ciliary body in the region of the ligamentum pectinatum. This permitted seepage of aqueous humor into the suprachoroidal space, hence detachment of the choroid. Fuchs believed that transudation also occurred. O'Brien [16] (1936) found that the fluid as drawn from beneath such a detachment was albuminous, contained fibrin and some red blood cells, and coagulated rapidly. He concluded that it was derived from the blood and not from the aqueous humor.

Meller (1912) propounded the following theory as to causation: Loss of aqueous humor is followed by reduced intraocular pressure, which gives rise to transudation from the vessels of the ciliary body and loss of fluid from the vitreous humor. When enough fluid accumulates in the suprachoroidal space and the pressure becomes great enough, the choroid is detached. Verhoeff [21] (1925), similarly, believed that the prime etiologic factor was a marked decrease in intraocular pressure. He likewise felt that transudation of fluid from the choroidal vessels distended the suprachoroidal space and caused serous choroidal detachment by dissecting the choroid from the sclera.

Kirby [13] (1950) felt that surgical manipulation over the sclera may increase the degree and frequency of detachments of the choroid. That trauma is a likely factor is an opinion shared by Spaeth [19] (1944), who doubts whether an anatomic detachment of the choroid from the sclera ever occurs except as a result of trauma.

Villaseca [23] (1954) stated: "Choroidal detachment is caused by the traction which the vitreous humor, prolapsed into the anterior chamber, exerts on its base, or origin, in front of the ora serrata." He did not insist that this is the only cause of choroidal detachment, but stated that internal vitreous

Received for publication Oct. 17, 1955.

From the Research Department of the Wills Eye Hospital. U. S. Public Health Research Fellow of the National Institute of Neurologic Diseases and Blindness (Dr. Capper).

* References 10 and 11.

herniation is the most frequent etiology of serous choroidal detachment in intracapsular cataract extraction.

Bellows [2] (1955), in discussing the flattened anterior chamber, stated:

> When the dam-like effect of the hyaloid and the vitreous is in full operation, the accumulation of regenerated aqueous eventually results in a backward-pressure effect, which interferes with the circulation in the ciliary processes, causing a reduction in aqueous formation. Eventually, the circulation to the iris itself is involved, with a corresponding drop in the output of aqueous from its anterior surface. It is likely that the circulatory disturbance in the ciliary processes, by backward extension, finally causes a similar stagnation and edema in the venous channels of the choroid. This leads to transudation into the suprachoroidal space and elevation of choroid, a frequent accompaniment of flat chamber.

Other reports of note were made by Rheuling (1870), Groenouw (1889), Haab (1893), Lindermann (1893), Marshall (1896), Hudson (1914), Barkan (1915), Meesmann [14] (1921), Hagen (1921), O'Brien [16] (1935), Lindner (1936), and Fronimopoulos [9] (1942). In general, it was believed that serous choroidal detachment was due to ocular hypotonia from wound leakage, with subsequent transudation of fluid from the choroidal vessels. Once the pressure from the transudate became great enough, the choroidal coat was forced to separate from the sclera.

APPEARANCE AND INCIDENCE

An eye presenting a serous choroidal detachment following intraocular surgery usually shows the following characteristics: There may be folds in Descemet's membrane, and usually a shallow or flat anterior chamber. The tension is soft or low-normal, and occasionally there is a demonstrable leakage of aqueous humor from the corneoscleral wound. Through a widely dilated pupil the detachment may be visible by oblique illumination. It appears as a dark-gray-brown mass behind the lens. On ophthalmoscopy the mass is seen to be a smooth, rounded swelling, extending hemispherically into the vitreous humor. The lesion may be single or multiple and usually arises anterior to the equator on either side of the midline. The borders are dark and well defined. The retinal vessels appear normal as they course over the elevated lesion. A serous choroidal detachment may be seen within several hours after surgery and usually persists for several days to two weeks.

Fuchs (1900) gave the incidence of choroidal detachment as 4.7% following cataract extraction and as 10% after simple iridectomy. Meller (1911) found 22% after sclerectomy. Hagen (1921) reported 22% detachments in a series of cataract extractions and 76% after corneoscleral trephine for glaucoma. O'Brien (1936) published an analysis of a large series of cataract extractions. He was able to view the fundus in 92 of 140 cases of cataract extraction of various types and found that 86 (93%) showed serous choroidal detachment. He reasoned that the previous low-incidence values were due to failure to examine the eye early and carefully enough after operation.

Fronimopoulos [9] produced, experimentally, anterior chamber fistulas in dogs and rabbits. He found ophthalmoscopic evidence of serous choroidal detachment within several hours after operation in approximately 66.7% of cases.

EXPERIMENTAL INVESTIGATION

The present studies were constructed in an effort to yield knowledge of the physiologic and pathologic alterations which are responsible for serous choroidal detachment following intraocular surgery. Most clinicians and previous investigators believe that the soft, or hypotonic, eye is the prime etiologic factor producing this complication. Based on this assumption, the first part of the experiment dealt with a series of rabbit eyes made hypotonic by means of a corneal fistula. Great care was taken not to traumatize the sclera so that hypotony and a flat anterior chamber would be the only factors affecting the choroidal coat.

A second series of experiments was devised in which normotensive rabbit eyes were subjected to scleral trauma by various surgical techniques in an effort to evaluate this

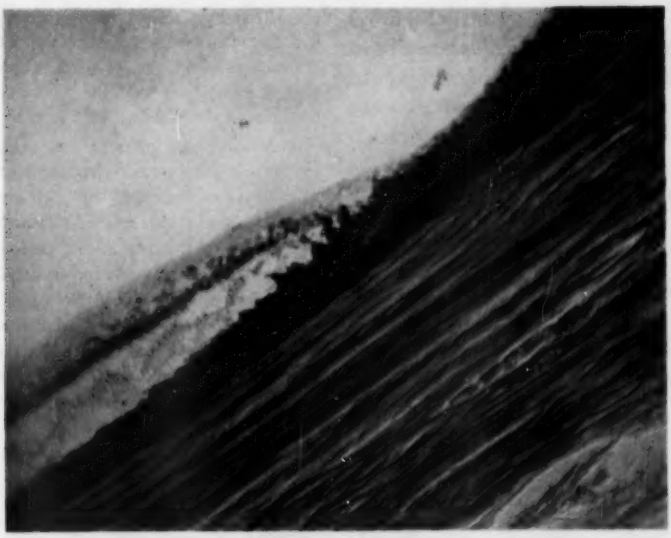
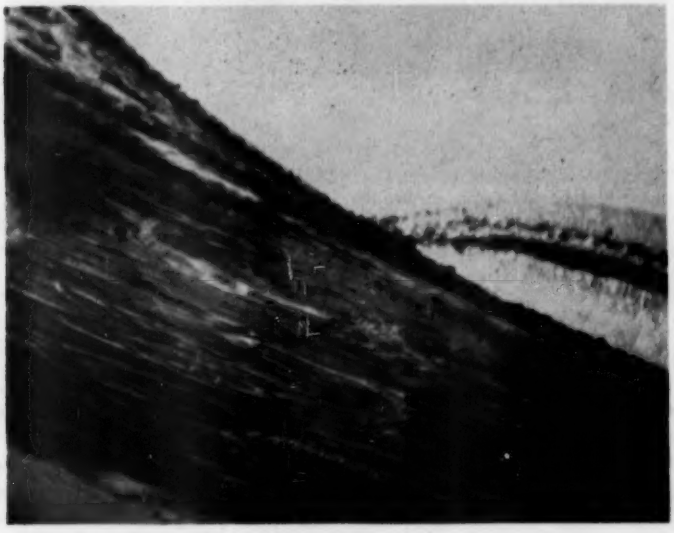


Fig. 1.—Section through the ora serrata of a normal rabbit eye.

factor in the production of choroidal detachment.

Since both the above factors, hypotony and scleral trauma, are present in any intraocular surgery, a third experiment was arranged combining the two conditions in another series of rabbit eyes. In addition, a series of normal rabbit eyes were enucleated and studied histologically. This gave a base line for comparison with the serous choroidal detachments found experimentally. The normal histology demonstrated the many artifacts of tissue preparation from which the true pathology had to be differentiated. Figures 1 and 2 are sections through a normal rabbit eye, showing the normal relationship

Fig. 2.—Section through the ora serrata of a normal rabbit eye.



of the sclera, choroid, and retina. Figure 3 demonstrates an artifactitious detachment of the choroid from the sclera. Suprachoroidal lamellae are present, but the homogeneous transudate is not present in the suprachoroidal space. This feature differentiates the pseudodetachment from the true detachment.

Experiment I: Hypotony and Flat Anterior Chamber

Procedure.

Throughout the experiment pigmented rabbits weighing approximately 2 kg. each were used. For any surgical procedure other than enucleation retrobulbar anesthesia was employed, using 0.50 cc. of 2% procaine hydrochloride. When an enucleation was to be performed, the rabbit was given in addition 1.0 grain (60 mg.) of pentobarbital sodium (Nembutal sodium) by the intravenous route.

The hypotony and the flat anterior chamber were created by means of a corneal fistula. A 3 to 4 mm. keratome incision was made through the sclera at 12 o'clock, 1 mm. from the limbus and parallel to it. A 2 to 3 mm. right-angled extension was cut at either extremity of the initial incision. The extensions were made with scissors and were directed toward the center of the cornea. The rectangular flap of cornea was then excised by making a fourth cut parallel to the keratome incision. Great care was taken not to traumatize the sclera surgically during this procedure. When fixation was required, only light conjunctival or superior rectus muscle fixation was utilized.

This procdeure allowed the aqueous humor to escape and the anterior chamber to remain flat for several hours before fibrin or iris obstructed the fistula. When it was desired to maintain the fistula for longer than three hours, periodic removal of fibrin or gentle manipulation of the iris away from the wound was necessary. Because of the extreme softness of the eyes, control of the intraocular tension by tonometry was impossible. However, it was felt that, by keeping a flat anterior chamber in all cases, the globes would be of fairly uniform softness.

In most cases the cornea remained clear enough for several days to permit careful inspection of the fundus for any evidence of serous choroidal detachment. Phenylephrine (Neo-Synephrine) hydrochloride, 10%, was used to dilate the pupils for periodic ophthalmoscopic examination. If serous choroidal detachment was observed, the eye was enucleated for histologic confirmation. At the end of five to seven days all remaining eyes were enucleated and prepared by the celloidin technique for histologic section. Representative sections were taken throughout the entire globe and stained with hematoxylin and eosin for microscopic study.

Fig. 3.—Section through the ora serrata showing artifactitious detachments of the choroid and retina.

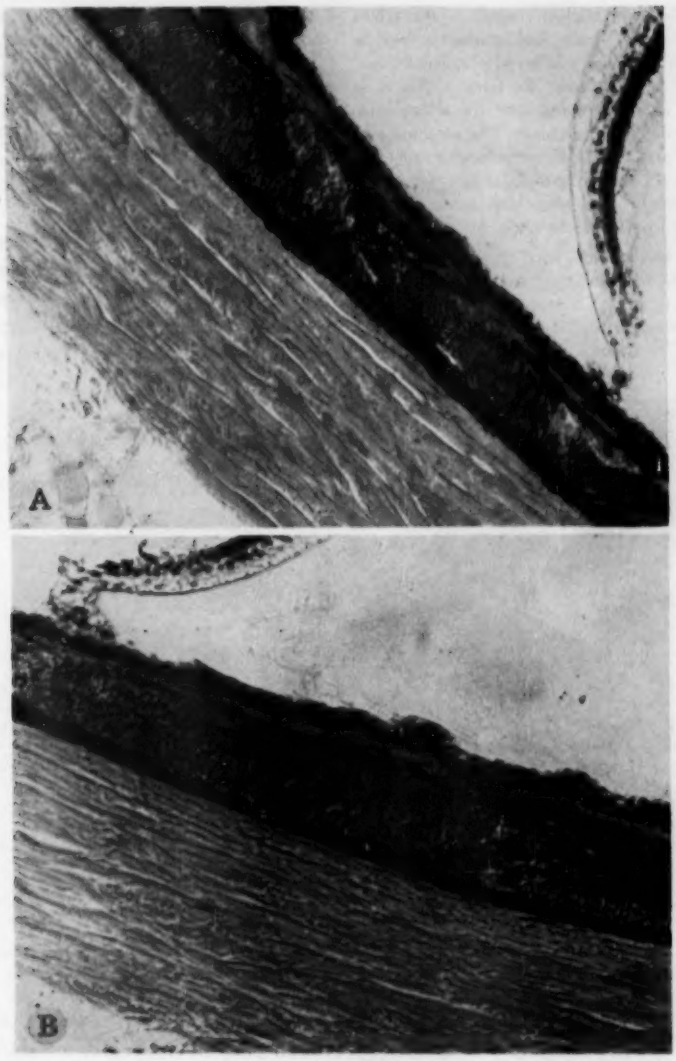


Fig. 4.—Sections through the ora serrata of rabbit eyes made hypotonic by means of a corneal fistula. The retinal detachment is an artifact.

Results.

In this experiment not one of the hypotonic eyes showed ophthalmoscopic evidence of serous choroidal detachment. Only 1 eye in 20 (5%) subjected to hypotony revealed histologic evidence of serous choroidal detachment. The detachment was flat and was situated superiorly near the equator.

The striking histologic feature was the tremendous hyperemia (dilatation and engorgement) of the entire uveal tissue, especially the choroid. This is well demonstrated in Figure 4. Note that the choroid is closely adherent to the sclera.

Experiment II: Scleral Trauma in Normotensive Eyes

Procedure.

In this series of rabbit eyes the globe was traumatized intentionally by various surgical techniques.

Hence, the effect of surgical trauma to the sclera overlying the ciliary body and choroid could be studied in eyes that were otherwise normal. Two methods were used to create the trauma. The first was merely a gentle scraping over the sclera after a conjunctival flap had been made. The scraping was done with a Bard-Parker blade several millimeters anterior to the equator at 12 o'clock. The sclera was thinned out over a 3×4 mm. area until the dark color of the choroid could be seen.

The second method was so arranged as to simulate the trauma of a cataract extraction, with the exception of entering the anterior chamber. A limbus-based conjunctival flap was dissected down from above. Then, with a Bard-Parker knife, a scratch incision was made halfway through the sclera, 1.5 mm. behind the limbus. The incision was continued over the upper half of the globe for 180 degrees. Three preplaced corneoscleral sutures were inserted and tied, all without entering the anterior chamber. The conjunctival flap was then closed with a single running suture.

As in Experiment I, these eyes were observed periodically for five to seven days for ophthalmoscopic evidence of serous choroidal detachment. Then enucleations were made for histologic confirmation of the clinical findings.

Results.

It was thought that 1 of the 23 eyes thus treated showed ophthalmoscopic evidence of serous choroidal detachment in the region traumatized. However, histologic examination revealed no serous detachment in any of the eyes. Two eyes in the series did show a small sanguineous detachment in the area of trauma; one of these explained what was thought to have been a serous detachment ophthalmoscopically.

Again, the striking feature seen histologically was the tremendous hyperemia (dilatation and engorgement) of the choroidal coat. However, in this series the hyperemia was localized chiefly to the region traumatized.

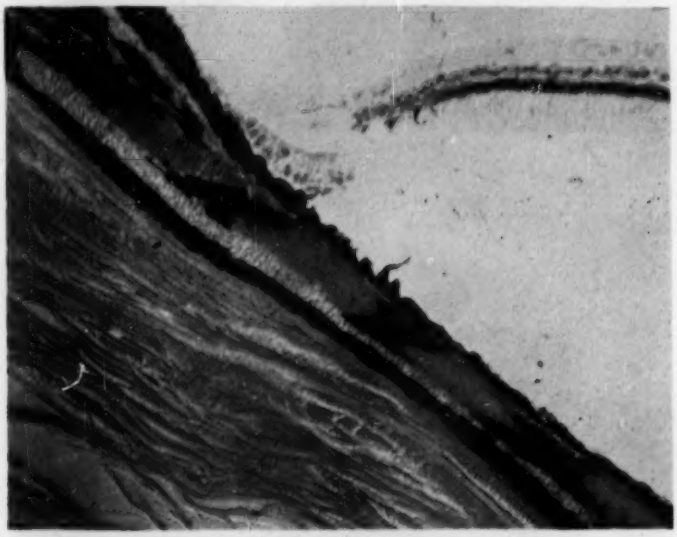


Fig. 5.—Section through the ora serrata of a rabbit eye subjected to scleral trauma in the region described above. The retinal detachment is an artifact of preparation.

Figure 5 demonstrates the hyperemic choroidal coat in the region of scleral trauma. The choroid and sclera were also closely adherent in this series.

EXPERIMENT III: COMBINATION OF HYPOTONY AND TRAUMA IN THE SAME EYE

Procedure.

The procedure in this group of rabbits was a combination of the technique used in Experiments I and II, i. e., surgical trauma over the sclera and hypotony produced by means of a corneal fistula. The two procedures were combined in each eye of this series in the order mentioned above.

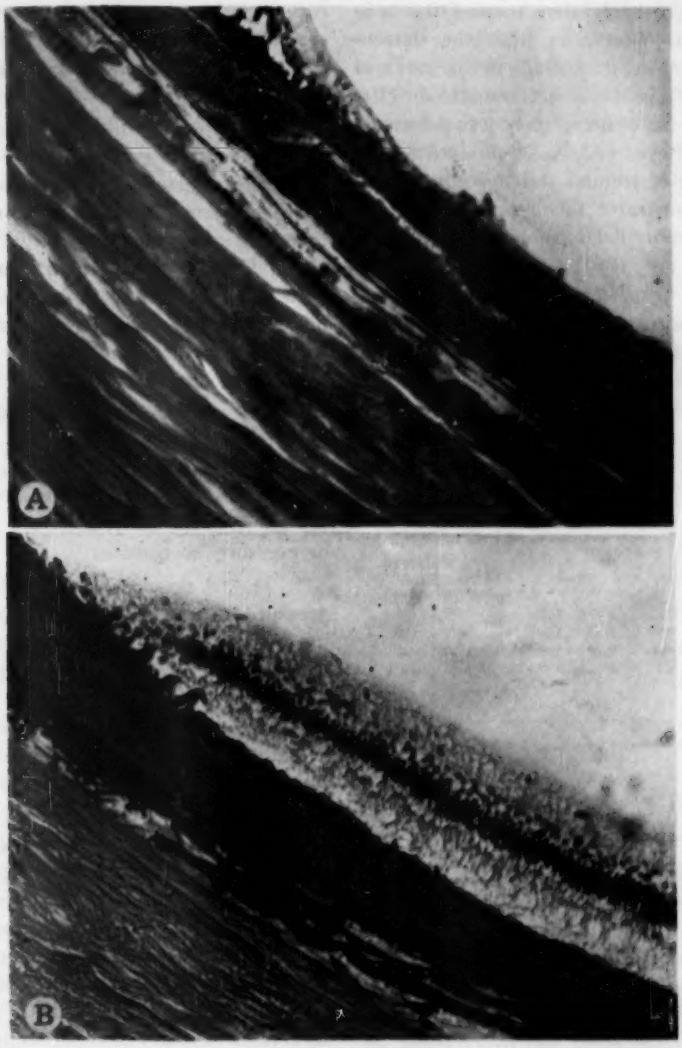


Fig. 6.—Sections through the ora serrata of rabbit eyes subjected to a combination of scleral trauma and hypotony. Note the serous choroidal detachment.

Results.

Periodic ophthalmoscopic examination of these eyes revealed a serous choroidal detachment in 9 of the 24 (37.5%) eyes thus treated. However, an accurate fundal survey of this group was not always possible because of the striate keratopathy and edematous clouding of the cornea that frequently occurred. In these instances evidence of serous choroidal detachment depended solely on histologic study, which was performed on all eyes regardless of whether or not ophthalmoscopy was possible.

The choroidal detachments were of serous nature and fairly flat. They appeared as a dark-brown, gently curved elevation, with the convexity directed toward the nerve head. The borders were dark and well defined. The normal retinal vessels coursed over the surface of the lesion.

Microscopic study corroborated the ophthalmoscopic observation that the detachments occurred chiefly (95% in this series of experiments) in the area traumatized. Histologic evidence of detachment was present in 19 of the 23 eyes (82.6%) subjected to this combination of trauma and hypotony. Figure 6 demonstrates the hyperemic choroid and serous choroidal detachment.

COMMENT

Serous choroidal detachment was not seen in the histologic examination of 15 normal rabbit eyes. Many artifacts were seen, but none showed the homogeneous, pink-staining, protein-rich transudate between the choroid and the sclera that is indicative of serous choroidal detachment.

TABLE 1.—*Incidence of Serous Choroidal Detachment*

	Ophthalmoscopic Study		Histologic Study	
Normal eyes	0/15*	(0%)	0/15	(0%)
Traumatized eyes	1/23	(4.4%) †	0/23	(0%)
Hypotonized eyes	0/20	(0%)	1/20	(5%)
Combination of trauma and hypotony	9/24	(37.5%)	19/23	(82.6%) ‡

* No. of serous choroidal detachments detected/no. of eyes studied.
† Sanguineous detachment.
‡ One eye lost.

As shown in Table 1, none of the eyes subjected to trauma alone showed serous choroidal detachment, and only 5% of the eyes subjected to hypotony showed this complication. However, 82.6% of the eyes that were both traumatized and hypotonized developed detachments. The fact that neither factor (trauma or hypotony) alone, but the two together, induced serous detachments poses the interesting question as to the cause. The following theory is proposed as a probable explanation of the mechanism of serous choroidal detachment.

Mechanism.—This theory is based on the manner in which local edema is produced anywhere in the body, stressing the reaction of the blood vessels and capillaries to abnormal stimulation or environment, with application of this knowledge to the choroid. In the case of intraocular surgery the abnormal stimulation is twofold: first, trauma of surgical manipulation over the sclera; second, hypotony.

The experiments described have shown that neither factor alone can produce serous choroidal detachment in the numbers seen following intraocular surgery. We must conclude, therefore, that trauma or hypotony, occurring alone, is a subthreshold stimulus, but the two together provide an adequate stimulus for the production of serous choroidal detachment.

In order to explain what actually occurred to bring about the detachment, the forces normally acting upon the intact globe (especially the choroid) must be reviewed. As elsewhere in the body, there are three forces or pressures to consider.

1. The tissue pressure, or the intraocular pressure, is one of the three forces affecting the choroidal coat. In this discussion we shall employ an intraocular pressure of 25 mm. of mercury (Schiøtz) as the normal tissue pressure exerted upon the choroidal vessels. This force tends to act against transudation of fluid from the vessels.

2. The second pressure factor influencing the ocular tissues is the intravascular pressure, or blood pressure. Since transudation occurs chiefly at a capillary level, we shall limit the discussion to the choroidal capillaries, but not necessarily the choriocapillaris. Although the actual intraocular capillary blood pressure has never been determined, an arterial capillary blood pressure of 32 mm. of mercury and a venous capillary blood pressure of 12 mm. of mercury are generally accepted (Adler). This force tends to cause transudation from the choroidal capillaries into the tissues.

3. The last intraocular force to be considered is the oncotic pressure, or colloid osmotic pressure. This is an osmotic force exerted by the protein colloids of the plasma and tends to draw fluid from the tissues into the vascular tree. The oncotic force is especially active at the venous end of the capil-

laries, where the plasma is more concentrated in colloids.

To recapitulate: The intraocular pressure, the intracapillary blood pressure, and the oncotic pressure are in equilibrium in the normal eye. By analyzing each experiment in turn, it can be shown how one or more of these forces is altered and allows for transudation of fluid in the suprachoroidal space, giving rise to serous choroidal detachment.

By adding the forces tending to increase transudation and comparing the result with the sum total of forces counteracting the transudation, one arrives at a result indicating in which direction fluid will flow. This resultant force must be calculated at both the arterial and the venous end of the system, and then the two are compared for an overall result. Since fluid transudate from the arterial end of the capillary tends to reenter the vascular bed at the venous end without the aid of lymphatics (there are no lymphatic channels within the eye), the calculations are much simplified. Figure 7 is a diagrammatic representation of how the ocular pressure systems were altered in this series of experiments.

As indicated in Table 2, in the normal eye, there is an intraocular pressure of 25 mm. of mercury acting to force fluid back into the arterial capillaries. This is opposed by the capillary blood pressure of 32 mm. of mercury tending to force fluids out of the arterial capillaries. There is, therefore, a pressure gradient of 7 mm. of mercury which causes extravasation of fluid at the arterial side of the capillaries.

At the venous side of the capillary bed, the intraocular pressure is still 25 mm. of mercury acting to keep fluids within the venous capillaries. The oncotic pressure also tends to keep the fluids within the capillary bed at the venous side. This is of the magnitude of 25 mm. of mercury. The oncotic pressure acts chiefly at the venous end because of the concentration of plasma proteins which occurs when the water and crystal-

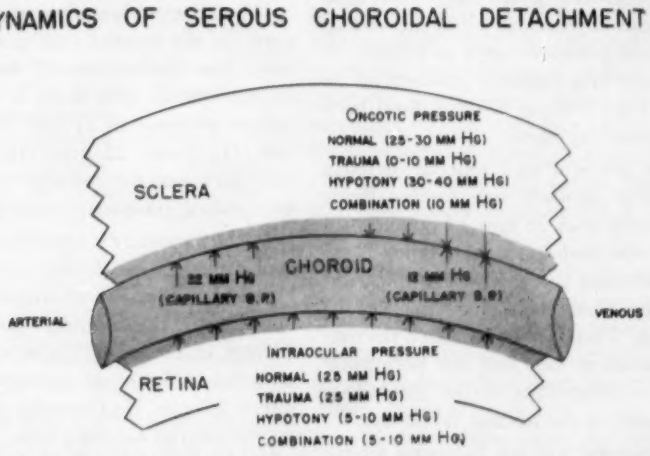


Fig. 7.—Distribution of the various pressures within the normal eye and how these were altered following (1) scleral trauma, (2) hypotony, and (3) a combination of scleral trauma and hypotony.

TABLE 2.—*Resultant Forces Acting in the Normal Eye*

	Arterial		Venous	
	In	Out	In	Out
Intraocular pressure	25	—	25	—
Capillary B. P.	—	32	—	12
Oncotic pressure	—	—	25	—
	25	32	50	12
Result:	Force of 7 mm. Hg causing extravasation of fluid		Force of 38 mm. Hg drawing fluid back into circulation	

TABLE 3.—*Resultant Forces Acting in the Hypotonic Eye*

	Arterial		Venous	
	In	Out	In	Out
Intraocular pressure	10	—	10	—
Capillary B. P.	—	32	—	12
Oncotic pressure	—	—	35	—
	10	32	45	12
Result:	Forces of 22 mm. Hg causing extravasation of fluid		Forces of 33 mm. Hg drawing fluid back into circulation	

loids are forced out at the arterial side. There is therefore a total pressure of 50 mm. of mercury (the intraocular pressure and the oncotic pressure), which forces fluid back into the venous capillaries. Since the venous capillary blood pressure drops to 12 mm. of mercury, there is a pressure gradient of 38 mm. of mercury tending to draw fluid back into the venous capillaries.

When the gradient of 7 mm. of mercury on the arterial capillary side forcing fluids out is compared with 38 mm. of mercury on the venous side tending to draw fluids back, there is a resultant force of 31 mm. of mercury drawing fluids back into the venous capillary bed. This allows for much fluctuation and variation, but still not permitting transudate to accumulate within the suprachoroidal space of the normal rabbit eye.

In the hypotonic eye the following alterations occur, and the resultant forces are calculated similarly to those changes that occur in the normal eye. In the hypotonic eye the intraocular pressure drops to 10 mm. of mercury, which is the only force counteracting extravasation of fluid at the arterial side of the capillaries. Opposing this is the arterial capillary blood pressure of 32 mm. of mercury. There is, therefore, a resultant pressure gradient of 22 mm. of mercury (32 mm. Hg minus 10 mm. Hg) causing extravasation of fluid at the arterial capillaries.

At the venous capillary bed, the forces tending to draw fluid back into the vascular tree are the intraocular pressure of 10 mm. of mercury and an oncotic pressure of 35 mm. of mercury. Therefore, there is a resultant force of 45 mm. of mercury (10 mm. Hg plus 35 mm. Hg) drawing fluid back into the venous capillaries. The large rise in oncotic pressure is due to the increased outflow of water and crystalloids at the arterial side, which is enhanced by the low intraocular pressure. Thus the colloids are greatly concentrated on the venous capillary side. The only force opposing the pressures causing an influx of fluid is the venous capillary blood pressure of 12 mm. of mercury. In the venous side there is, therefore, an over-all force of 33 mm. of mercury (45 mm. Hg minus 12 mm. Hg) causing an influx of fluid into the venous capillaries.

When the outflow force of 22 mm. of mercury, on the arterial side, is compared with the inflow tendency of 33 mm. of mercury, on the venous side, there is an over-all resultant pressure of 11 mm. of mercury (33 mm. Hg minus 22 mm. Hg) which draws fluid back into the vascular tree. Hence still no residual transudate occurs.

In the surgically traumatized eye the intraocular pressure of 25 mm. of mercury keeping fluid within the arterial capillary bed is opposed by the capillary blood pressure of 32 mm. of mercury. There results an over-all force of 7 mm. of mercury (32 mm. Hg minus 25 mm. Hg) causing outflow of fluid on the arterial capillary side.

On the venous side the intraocular pressure of 25 mm. of mercury remains the same. However, the oncotic pressure drops to 10 mm. of mercury, as a result of the trauma to the capillaries of the choroidal coat. This allows the colloidal proteins to leak into the tissues; thus the oncotic pressure is reduced.

TABLE 4.—*Resultant Forces Acting in the Traumatized Eye*

	Arterial		Venous	
	In	Out	In	Out
Intraocular pressure	25	—	25	—
Capillary B. P.	—	32	—	12
Oncotic pressure	—	—	10	0
	25	32	35	12
Result:	Force of 7 mm. Hg causing extravasation of fluid		Force of 23 mm. Hg drawing fluid back into circulation	

especially at the venous side, where it exerts most of its effect. There is therefore an over-all effect of 35 mm. of mercury (25 mm. Hg plus 10 mm. Hg) forcing fluid into the venous capillaries. This is opposed by the venous capillary blood pressure of 12 mm. of mercury. The resultant of the forces on the venous side is 23 mm. of mercury (35 mm. Hg minus 12 mm. Hg) causing an influx of fluid.

When the resultant forces at the arterial side of 7 mm. of mercury causing extravasation are compared with those at the venous side of 23 mm. of mercury causing an influx of fluid, the total resultant of all the forces is 16 mm. of mercury (23 mm. Hg minus 7 mm. Hg). This resultant gradient of pressure acts to cause fluid to flow back into the venous capillaries. Here, again, it is demonstrated that no fluid will accumulate in the suprachoroidal space.

TABLE 5.—*Resultant Forces Acting in the Eye Subjected to Both Surgical Trauma and Hypotony*

	Arterial		Venous	
	In	Out	In	Out
Intraocular pressure	10	—	10	—
Capillary B. P.	—	32	—	12
Oncotic pressure	—	—	10	—
	10	32	20	12
Result:	Force of 22 mm. Hg causing extravasation of fluid		Force of 8 mm. Hg drawing fluid back into circulation	

In the eye surgically traumatized and made hypotonic the following results are calculated: On the arterial side of the capillary bed the only force keeping fluids within the vascular tree is an intraocular pressure of 10 mm. of mercury. This is opposed by an arterial capillary blood pressure of 32 mm. of mercury. There is thus a calculated resultant force of 22 mm. of mercury (32 mm. Hg minus 10 mm. Hg) causing extravasation of fluid.

On the venous side the forces acting are the intraocular pressure of 10 mm. of mercury and an oncotic pressure of 10 mm. of mercury. Again, the oncotic pressure is markedly reduced because of the traumatized capillaries. Thus, there is a total of 20 mm. of mercury acting to keep fluid within the vascular tree on the venous side. Opposing this is the venous capillary blood pressure of 12 mm. of mercury. On the venous side there is therefore a resultant force of 8 mm. of mercury (20 mm. Hg minus 12 mm. Hg) drawing fluid back into the capillary bed.

Thus it can be seen that the total resultant pressure gradient would be 22 mm. of mercury from the arterial capillary bed causing extravasation as compared with 8 mm. of mercury from the venous capillary bed tending to oppose the extravasation. There would be an over-all resultant force of 14 mm. of mercury (22 mm. Hg minus 8 mm. Hg) producing transudation of fluid in the suprachoroidal space, hence serous choroidal detachment. From this last experiment, and the calculation of its results, there is a reasonable indication of why serous choroidal detachment occurs so frequently in intraocular surgery.

It would be reasonable to assume that removal of the abnormal environment or stimuli, permitting the physiologic forces to realign themselves again within the globe, should facilitate the obliteration of the detachment. Perhaps, then, the serous choroidal detachment recedes once the wound heals without leakage and the injury from the surgical manipulation subsides. This usually takes place in several days or, occasionally, weeks. Should the detachment persist for an unreasonable length of time, then some of the other complications should be suspected.

Probably one of the commonest reasons for a serous choroidal detachment not receding rapidly is persistence of a small aqueous fistula. If this cause can be ruled out, it is possible that a sanguineous choroidal detachment may be the etiologic factor. The latter complication may take months to resorb, or it may persist owing to organization of the blood in the suprachoroidal space. Two other complications which must be considered in the differential diagnosis are

serous retinal detachment and the appearance of a tumor, especially the malignant melanoma. The diagnosis is usually made without too much difficulty with the various measures at hand today, namely, careful ophthalmoscopy, transillumination, radioactive phosphorus studies, and, possibly, a diagnostic puncture over the site of the lesion.

There are types of choroidal detachment other than serous which may be mentioned but fall outside the limits of this paper. Sanguineous choroidal detachment may follow surgery, or it can even occur spontaneously, as a result of vascular disease. Inflammatory disease within the globe may also cause choroidal detachment by scarring and contracture. A lacrimal gland tumor, pressing on the intact globe, has been reported to have simulated a choroidal detachment, which disappeared with removal of the tumor (Ziporkes [28]).

SUMMARY

A brief review of the literature on the subject of serous choroidal detachment is presented. In the past, it has been the consensus that hypotony (probably from a leaking corneal wound) was the prime etiologic factor in the production of these detachments. It is suggested by these studies that surgical trauma is an equally important factor and that both trauma and hypotony are necessary in order for this complication to occur. With this in mind, histologic sections through normal rabbit eyes were studied as a base line for comparison. Three experiments were conducted to show the effects of (1) hypotony, (2) scleral trauma, and (3) a combination of scleral trauma and hypotony. None of the normal eyes showed histologic evidence of serous choroidal detachment, nor did any of the eyes subjected to trauma alone exhibit this condition. Only 5% of the eyes made hypotonic showed histologic evidence of detachment. Of the eyes subjected to both scleral trauma and hypotony, 37.5% showed ophthalmoscopic evidence and 82.6% showed histologic confirmation of serous choroidal detachment. The area of greatest surgical trauma seemed to localize the region in which the detachments occurred. In this series of experiments it was found that 95% of the serous choroidal detachments occurred in the region of the surgical trauma.

A theory is proposed to explain the physiologic basis for serous choroidal detachment. By showing how the above experiments altered the normal pressure relationships within the choroid (intracapillary blood pressure, intraocular pressure, and oncotic pressure), a logical explanation could be given for the combination of hypotony and scleral trauma, and not either alone, as a cause of serous choroidal detachment.

CONCLUSIONS

1. Both surgical trauma and hypotony are prerequisites for the experimental production of serous choroidal detachment following intraocular surgery.

2. Experimental serous choroidal detachment does not seem to occur in the presence of surgical trauma alone or hypotony alone.

3. Surgical trauma appears to have a localizing influence on the site in which serous choroidal detachment will occur.

REFERENCES

1. Barkan, H.: Postoperative Detachment of the Choroid with Special Reference to Elliot's Operation for Glaucoma, J. A. M. A. **65**:1520, 1915.

2. Bellows, J.; Lieberman, H., and Abrahamson, I.: Flattened Anterior Chamber, A. M. A. Arch. Ophth. **54**:170, 1955.

3. Bothman, L., and Blaess, M. J.: Results of the Surgery of Glaucoma, Am. J. Ophth. **19**:1072, 1936.

4. Bothman, L.: Repair of Choroidal Detachment: Report of a Case, Arch. Ophth. **18**:65, 1937.

5. Collins, E. T.: Contusion Hypotony, Tr. Ophth. Soc. U. Kingdom **37**:281, 1916; **38**:217, 1917.

6. Csillag, F.: Early Post-Operative Detachment of Choroid, Brit. J. Ophth. **33**:694, 1949.

7. Darby, G. S.: Late Post-Operative Separation of the Choroid, Arch. Ophth. **4**:530, 1930.

8. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. III, St. Louis, C. V. Mosby Company, 1941, p. 2538.

9. Fronimopoulos, J.: Pathogenesis of Serous Choroidal Detachment, Klin. Monatsbl. Augenh. **108**:665, 1942.

10. Fuchs, E.: Ablösung der Aderhaut nach Operationen, von Graefes Arch. Ophth. **53**:395, 1902.

11. Fuchs, E.: Ablösung der Aderhaut, von Graefes Arch. Ophth. **51**:199, 1901.

12. Hudson, A. C.: Serous Detachment of the Choroid and Ciliary Body as an Accompaniment of Perforating Lesions of the Eyeball, Roy. Lond. Ophth. Hosp. Rep. **19**:301, 1914.

13. Kirby, D. B.: Surgery of Cataract, Philadelphia, J. B. Lippincott Company, 1950, p. 519.

14. Meesmann, A.: Experimentelle und anatomische Studien zur Frage der Aderhautabhebung, Arch. Augenh. **90**:69, 1921.

15. O'Brien, C. S.: Detachment of the Choroid After Cataract Extraction: Clinical and Experimental Studies, with Report of 75 Cases, Arch. Ophth. **14**:527, 1935.

16. O'Brien, C. S.: Further Observations on Detachment of Choroid After Cataract Extraction, Arch. Ophth. **16**:655, 1936.

17. Parker, A. E. P.: Bilateral Detachment of the Choroid of Unusual Duration Following Corneoscleral Trephine, Brit. J. Ophth. **30**:595, 1946.

18. Raycroft, B. W.: Choroidal Detachment, Brit. J. Ophth. **27**:283, 1943.

19. Spaeth, E. B., and DeLong, P.: Detachment of the Choroid: Clinical and Histologic Analysis, Arch. Ophth. **32**:217, 1944.

20. Verhoeff, F. H.: The Pathogenesis of Glaucoma, Arch. Ophth. **54**:20, 1925.

21. Verhoeff, F. H., and Waite, J. H.: Separation of the Choroid, with Report of a Spontaneous Case, Arch. Ophth. **55**:38, 1925.

22. Villaseca, A.: Late Emptying of Anterior Chamber and Choroidal Detachment in Cataract Operations, A. M. A. Arch. Ophth. **52**:250, 1954.

23. Ziporkes, J.: A Case of Mixed Tumor of the Lacrimal Gland, with Retinal Folds and Choroidal Detachment, Which Disappeared After Removal of the Growth, Arch. Ophth. **18**:933, 1937.

Clinical Notes, New Instruments and Techniques

USE OF THE BINOCULAR MICROSCOPE IN EYE OPERATIONS

HENRI M. DEKKING, M.D., Groningen, Netherlands

EVER SINCE the moment that the slit lamp with binocular microscope came into daily use, ophthalmology has suffered from a strange and troubling discrepancy. We examine the eye and make our diagnosis with a magnification of 10 to 40, and we would feel hopelessly inadequate if we had to rely upon the naked eye. As soon as we start to operate, however, we *do* have nothing but the naked eye to rely upon, and to guide us through movements which may mean happiness or disaster to our patient.

In this respect, our technique has not advanced one step beyond our grandfathers', and all too often we feel like the proverbial bull in the china shop. What exactly we have been doing is revealed only by our slit lamp, a week or so *after* the operation! It is quite obvious what the next step has to be: We shall have to operate, as we examine, under a magnification as high as feasible. The original binocular microscope as used with the slit lamp is not satisfactory for operations, because the free working distance is too small. A practical solution, however, has been found by the firm of Zeiss with the new form of microscope used in their latest slit lamp apparatus, which has been converted into an instrument for operations called the otoscope. In reality, this is a telescope with variable magnification, fitted with a fixed front lens of 5 D., thus having a fixed free working distance of 20 cm. at any magnification between 4 and 25 times. The change of magnification is obtained by a rotating drum of lenses, acting either as a minifying or as a magnifying system. This instrument, built originally for fenestration and other delicate ear operations, seems ideally suited for our purpose, too.

In practical use, however, my colleagues and I have found the original otoscope giving too much in one respect and too little in certain others. For eye operations, one single magnification is sufficient in all cases, and we found the best to be 10 ×. A smaller magnification is hardly worth while,

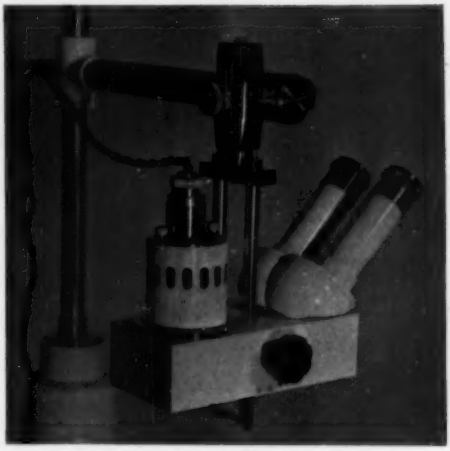


Fig. 1.—The microscope with built-in light source hanging on its support, which allows movements along three perpendicular axes.

and a higher one is not satisfactory because of insufficient depth of field. Now, with 12.5 × eyepieces, this magnification is obtained without any magnifying or minifying system in the path of rays. The elaborate and costly changing device, therefore, can be dropped altogether, thus permitting a much simpler and cheaper design.

On the other hand, the small light field, of 33 mm., proved difficult in eye operations. It amply covers the field of view (20 mm. in diameter), but often one has to look beside the microscope to find things outside the field of view: needles lying there, the ends of threads to be knotted, etc. If the room is dark, as it mostly is, the small circle of light yielded by the original instrument is a definite disadvantage. In our instrument, therefore, we used a larger condenser, giving a light field of 45 mm., and, after one year's experience, I feel this is still too small. It should be 50 mm. at least, to be really convenient.

A second disadvantage of the original instrument is its unwieldy stand, which, moreover, cannot be adjusted by the surgeon himself. In eye operations, it has proved absolutely essential that one be able to make small readjustments in any of the three

Submitted for publication June 14, 1955.

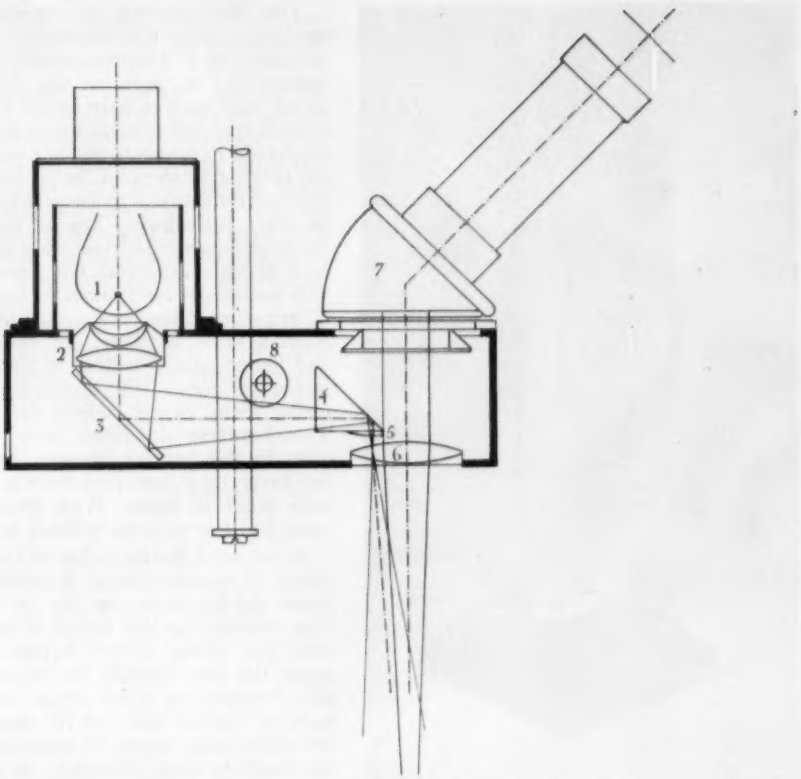


Fig. 2.—The essential parts of the instrument. The filament of the lamp (*1*) (same bulb as used in the Haag-Streit slit lamp) is imaged by the condenser (*2*) through the rear surface mirror (*3*), the prism (*4*), and the projector lens (*5*) on the achromatic objective lens (*6*). This lens "sees" the condenser mounting (*2*) at infinity through the lens (*5*) and therefore projects a sharply defined image of this mounting at its focal point. Thus, a round and evenly illuminated light field is formed at 20 cm., the place of the patient's eye. By the same lens (*6*) an image of the eye is formed at infinity, and this image is viewed through the binocular telescopic Zeiss eyepiece (*7*). At *8* are two conical, spring-loaded wheels engaging in slots in the steel bars (*9*) Thus, an absolutely even and smooth-focusing movement is possible, without any backlash.

directions while looking through the microscope without endangering the sterility of the hands. We built a stand, therefore, in which these adjustments can be made by the surgeon's feet (for two movements in the horizontal plane) and by his knee (for vertical displacements; Fig. 3).

By following the lines discussed above, one can build a simple and quite efficient instrument. Even then, however, one essential thing is lacking: a faultless fixation of the patient's head. With the ordinary headrest, continuous readjustments must be made during operation which seriously hamper the smooth course of the work and which tax unduly the surgeon's nerves. To be of any use, the operation microscope must be used in conjunction with a special headrest giving a gentle, but absolutely firm, fixation, so that at the end of the operation the patient's eye has not moved 1 mm. from its initial position in space. For readers who contemplate using the operation microscope, I cannot put enough stress on this point. One must start with a perfect headrest; without this, one will have nothing but irritation and disappointment.

Some years ago, we experienced the same difficulty when it came to filming eye operations. The headrest developed then proved excellent for microsurgery, too. It consists (Fig. 4) of a three-sided wooden box which fits into the existing headrest clamp of the operation table. The three sides of the box

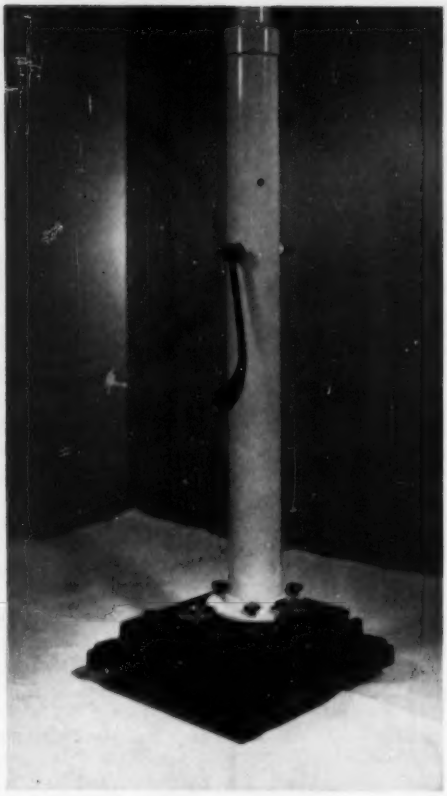


Fig. 3.—The base of the stand is an old Zeiss instrument carrier; the two wheels, for lateral and transverse movements, are rotated by the surgeon's foot; the lever halfway is for up-and-down movement adjustable by his knee.

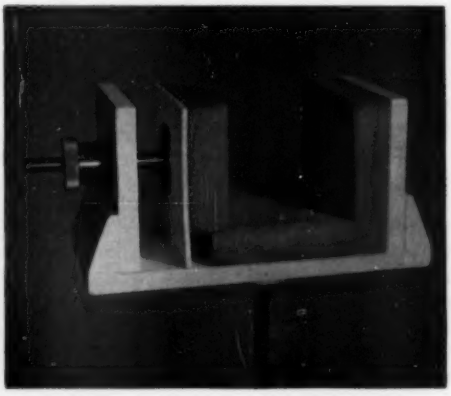
are padded with heavy foam rubber, and one of them can slide on a steel bar. This bar passes through a conical clamping device, so that, by a short turning movement of the locking nut, it can be tightened or loosened, thus fixing the sliding side in any desired position. In this way, a firm but gentle fixation of the patient's head is obtained, without giving him the panicky feeling of being immobilized and helpless.

In using the microscope, we discovered as an accessory, but very welcome, feature that the illuminating rays, emerging from the objective, and thus being almost parallel with the line of observation, give a bright red fundus reflex. One can operate, therefore, by diaphanoscopy, and this is extremely helpful in removing the last traces of a discissed lens, in needling tenuous secondary cataracts, and the like.

The first attempt to perform a major operation under this microscope will almost certainly be a disappointment. Just as our fathers had to learn to use the slit lamp, so we shall have to learn to use the operation microscope, and it takes many months to readjust our movements and our way of operating to this new medium. In the beginning, the greatest difficulty is to know where the ends of one's instruments are as soon as they have disappeared from the microscope's field of view, and one has continuously to look beside the instrument to find them and to introduce them back again into the field. After a while, however, one develops a new and better spatial feeling in the hands and learns to move the instruments, without seeing them, exactly where they should be. The headrest described here is a great asset in this respect, because one can lean the hands on it, and thus have a fixed reference point in space. With greater experience, one learns to do without it.

A second difficulty is that in certain movements it seems almost impossible not to insert the hands in the line of observation, thus obstructing the image of the patient's eye. The tilting of the Arruga forceps to grasp the lens capsule, for instance, invariably brought my hand before the objective lens, so that at this crucial moment, when the microscope would be most useful, nothing could be seen. However, in one way or another, one learns to overcome these difficulties (eventually by choosing an instrument of slightly different design) and begins to feel more confident. As the months pass by, one dares perform more and more while looking through the microscope, and has to look less beside the instrument at critical

Fig. 4.—Adjustable headrest.



stages, at which one has been accustomed for so many years to rely upon the naked eye.

A new feeling of assurance develops in the fingers, a new sense of space at tenfold magnification becomes a second nature; after a time not to use the microscope in operations becomes as unthinkable as not using it in diagnosis, and this is as it should be. At last it becomes possible to perform difficult operations with a subtlety, and a certainty of what one is doing, undreamed of before.

One thing, however, becomes constantly more apparent in doing microsurgery: how crude and clumsy even our finest instruments are as compared with the size and the textures of the eye itself. When this is remedied in the future—as it certainly will—and when the operation microscope has come into general use, as is the slit lamp today, we shall feel that a decisive new step has been taken toward a better and truly modern surgery of the eye.

SUMMARY

A description is given of a simplified and improved operation microscope based on the Zeiss otoscope, with a floor stand and a headrest designed especially for ophthalmic purposes. The difficulties and possibilities of microsurgery are discussed.

University Eye Clinic, Academisch Ziekenhuis.

Case Reports

SPONTANEOUS COMPLETE ABSORPTION OF A CATARACTOUS LENS

NORMAN CORIN, M.D., Jamaica, N. Y.

THE CASE to be reported is of interest because it presents an example of complete absorption of both a cataractous lens and its anterior capsule 29 years after development of a toxic cataract. It is also of interest that the patient was able to regain 20/20 corrected vision in spite of an amblyopia of such duration.

The literature records only five cases of spontaneous absorption of a cataractous lens, of which only two were in adults. The two adult cases were that of Ballantyne,[1] who reported in 1926 the spontaneous absorption of a cataractous lens with persistence of both anterior and posterior capsules in a 65-year-old woman, and that of Holloway and Cowan,[3] who reported in 1932 the case of spontaneous absorption of a luxated shrunken cataractous lens with a residual membranous rest in a 46-year-old man.

REPORT OF CASE

A married woman aged 45 was first seen by me on Aug. 10, 1949, and presented the following history: Twenty-three years previously the patient had had an acute iritis of the left eye. Six months after this episode she could perceive only light with the left eye. The past history relative to the right eye was negative. The condition of both eyes had remained *in status quo* from that time until the date of my first examination on Aug. 10. Examination at that time revealed a mature complete cataract in the left eye with no synechia. The eye was quiet, and the patient was symptom-free. The right eye was essentially negative. The visual acuity was 20/20 in the right eye and limited to light perception and projection in the left eye. The patient was again seen by me on Feb. 2, 1952, at which time presbyopic lenses were prescribed. There was no change in the left eye.

The patient returned on April 5, 1955, and stated that spontaneously on March 15, 1955, the left eye had become red and acutely painful. This condition persisted for a few days, after which there was marked photophobia. Examination revealed total aphakia. The anterior capsule and the lens had absorbed completely, and under the slit lamp fine, dust-like particles were seen on the anterior face of the vitreous. The visual acuity was 20/20 in the right eye and limited to finger counting at 3 ft. in the left eye. With a +7.25 sphere visual acuity was corrected to 20/20 in the left eye. Reexamination was performed on June 11 and Sept. 29. On both occasions the pupil was widely dilated with 10% phenylephrine (Neo-Synephrine). The dust-like particles on the anterior face of the vitreous have remained unchanged. Otherwise the vitreous is clear. No sign of the lens or its capsule was found in the vitreous after an exhaustive search with a widely dilated pupil. Tension in the left eye, as measured with the MacLean tonometer, has remained within normal limits. Corrected visual acuity is still 20/20. The eye has remained symptom-free to the present date.

87-12 175th St.

Received for publication Nov. 4, 1955.

REFERENCES

1. Ballantyne, A. J.: Brit. J. Ophth. **10**:202, 1926.

2. Ferrer, H.: Am. J. Ophth. **11**:886, 1928.

3. Holloway, H. M., and Cowan, A.: Arch. Ophth. **7**:332, 1932.

4. Vancea, P.: Arch. Ophth. **49**:78, 1932.

5. von Reuss, A. R.: Zentralbl. prak. Augenh. **24**:33, 1900.

VISUAL FUNCTION STUDIES IN A CASE OF LARGE ABERRANT VESSELS IN THE MACULA

DAVID VOLK, M.D., Cleveland

THE NORMAL distribution of the retinal nerve fibers and the retinal blood vessels is shown in Polyak's drawing (Fig. 1). It can be seen in the drawing that the macula is devoid of large vessels. This retinal vascular pattern may vary somewhat in the manner in which the vessels leave the disc and traverse the retina, but in no case have major vessels been reported to pass through the macula. The foveal area is free of any vessels.

REPORT OF CASE

Recently I observed an eye in which the macula was crossed by two large vessels, one arising from the inferior temporal vein and the other from the inferior temporal artery. The vessels were quite large and of the caliber of the vessels from which they arose. Within the macula the vein or venule divided into two branches, one extending laterally and slightly upward and the other laterally and slightly downward. Within the Y formed by the two branches, and very close to the point of bifurcation, was the fovea, which was distinguishable only by its color being darker than the surrounding macula, since no fovea reflex was present. Smaller branches from the macular vein and artery were seen to extend into the upper half of the retina.

The distribution of the vessels as described can be clearly seen in Figure 2, a photograph of the left fundus. The macula is outlined by its reflex. Figure 3, a photograph of the fundus of the right eye of the same patient, is shown for comparison. In it the distribution of the vessels is normal.

All other eye findings were normal except for a small refractive error in each eye. Correction for the right eye was +0.25 sph⌒—1.00 cyl, ax 180, with visual acuity of 20/15. Correction for the left eye was +0.50 sph⌒—1.25 cyl, ax 173, with visual acuity of 20/20.

To verify the position of the foveas, the blind spots were outlined on the tangent screen and were found to be slightly below the usual position for each eye, but within normal limits (Fig. 4). The Purkinje figure was then repeatedly elicited for each eye, and the patient was asked to make drawings of what she saw. Figure 5, the patient's drawings as copied by me, show, for the left eye, the large vessels as they leave the inferior temporal vessels and pass toward the fovea, to branch and surround the fovea, thus verifying the ophthalmoscopic appearance.

The central visual fields were studied on a tangent screen at a distance of 1 meter with a 1 mm. white test object. The origin and position of the aberrant macular vein were outlined, and they corresponded with the ophthalmoscopic appearance (Fig. 6).

COMMENT

To my knowledge, this is the first report of large macular vessels in an otherwise normal eye.* The presentation of this single instance of large vessels within the macula is sufficient to bring up for discussion several interesting points.

Visible retinal vessels, with individual variations, somewhat parallel the distribution of the retinal nerve fibers, with the inferior and superior temporal vessels arching below and above the macula. Since the retinal nerve fibers precede in development the retinal blood vessels, one might presume that metabolic factors within or near the nerve fiber layer govern the distribution of the large retinal vessels. The position of the macula lutea is indicated as early as the third embryonic month, whereas the retinal blood vessels first begin to develop in the embryo

Received for publication Oct. 31, 1955.

Presented at the East Central Section of the Association for Research in Ophthalmology, Buffalo, Jan. 10, 1955.

From the Western Reserve University School of Medicine and the Department of Surgery, Ophthalmological Service, of the University Hospitals of Cleveland.

* In his "Text-Book of Ophthalmology," Duke-Elder[1] states (p. 1387): "An artery derived from the inferior temporal vessel running directly over the macula was described by Nakashima (*Nip. gank. Zass.*, 1921).

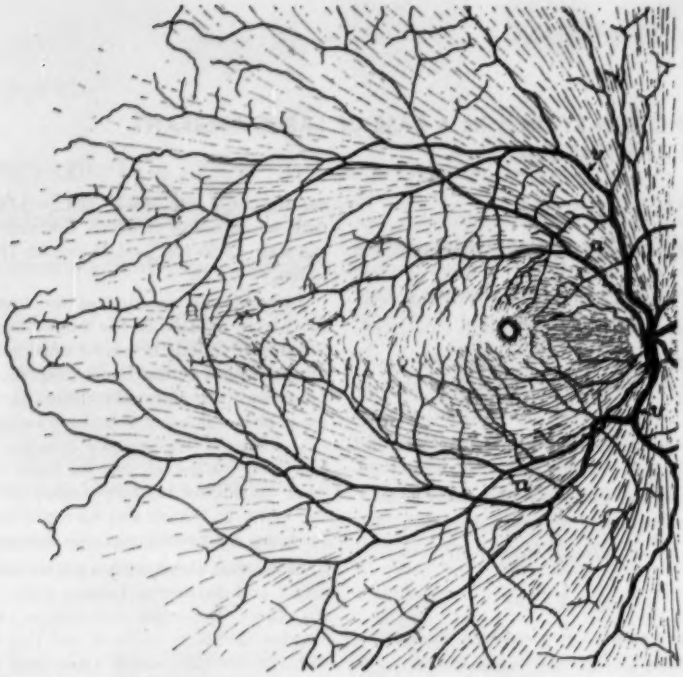


Fig. 1.—Normal distribution of retinal nerve fibers and retinal blood vessels (reproduced from Polyak, S.: The Retina, Chicago, University of Chicago Press, 1941).

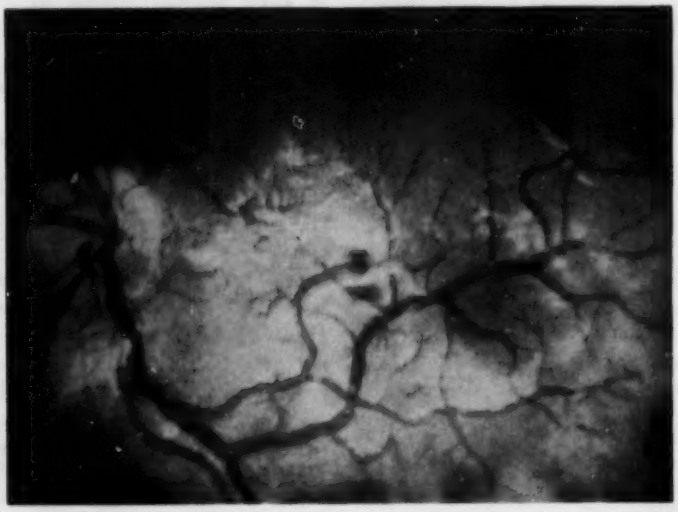


Fig. 2.—Photograph of the left fundus, in which large blood vessels can be seen within the macula.

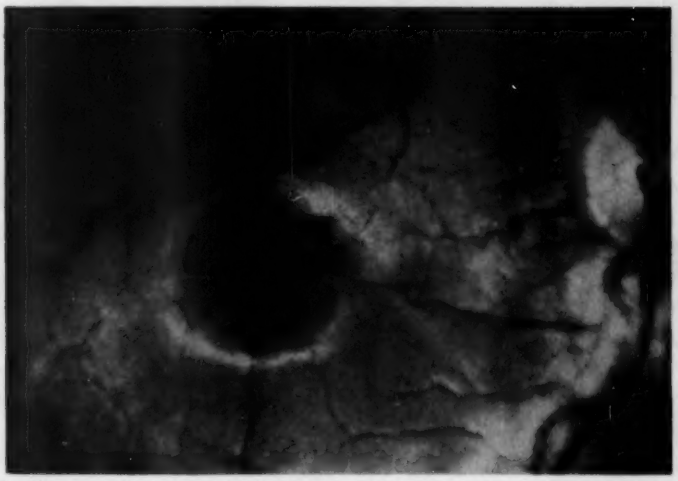


Fig. 3.—Photograph of the right fundus, in which the distribution of the blood vessels is normal.

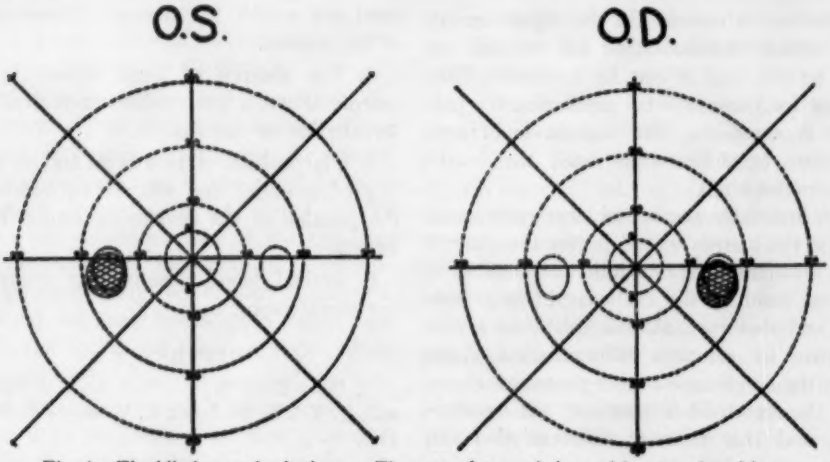


Fig. 4.—The blind spots for both eyes. They are of normal size and in normal position.

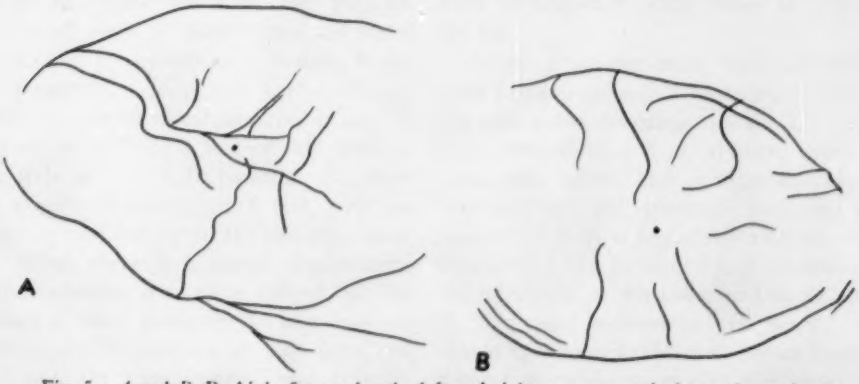


Fig. 5.—*A* and *B*, Purkinje figures for the left and right eyes, respectively, as drawn by the patient and copied by me. The central black dot represents the point fixated on a black tangent screen which the patient faced while the Purkinje figure was being elicited.

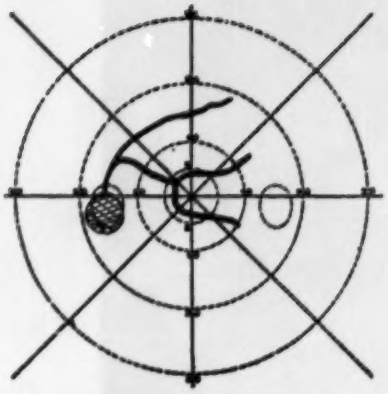


Fig. 6.—Origin and position of the aberrant vein as outlined on the tangent screen with a 1 mm. white test object at 1 meter.

at the fourth month. By the eighth month the retinal vascularization has reached the ora serrata and it can be concluded that, except for perhaps some capillaries, the pattern is complete. The macula and fovea continue to differentiate until the fourth month after birth.

An invariable absence of large retinal vessels in the macula would justify the concept that metabolic factors within the developing macula result in the exclusion of large vessels and that such absence might be a prerequisite for complete differentiation. However, the single case herein presented shows that the metabolic factors may not be absolute, and that macular differentiation can proceed normally despite the presence of large vessels within. Furthermore, the fovea has developed in its normal position despite the closeness of the large vessels. It can thus be concluded that the position of the macula and its fovea is predetermined and will not be altered by the position of the developing retinal blood vessels.

CONCLUSIONS

1. Some unknown metabolic factors govern the distribution of the developing retinal blood vessels, normally excluding large vessels from the macula.

2. Large retinal vessels may pass through the macula.

3. The presence of large macula vessels need not inhibit the normal differentiation of the macula.

4. The absence of large vessels in the macula is not a prerequisite to normal differentiation of the macula.

5. The position of the macula and its fovea is predetermined and will not be altered by the position of the developing retinal blood vessels.

6. Retinal blood vessels may cross the horizontal raphe.

REFERENCE

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. II, St. Louis, C. V. Mosby Company, 1938.

Annual Reviews

LIDS, LACRIMAL APPARATUS, AND CONJUNCTIVA

ALSON E. BRALEY, M.D., Iowa City

IN THE past two reviews an effort has been made to cover the literature as completely as possible without too much repetition of material. While it is impossible to review the literature on any subject without some repetition, an attempt has been made here to cover subjects which have not previously been completely reviewed.

THE LACRIMAL APPARATUS

Congenital Anomalies

Congenital anomalies and incomplete development of the collecting system of the lacrimal apparatus are common. Fazakas[1] says that the punctum should be at the most prominent point in the lid, where the lid crosses the semilunar fold of the conjunctiva, between this fold and the caruncle. The punctum may be displaced forward, backward, or more laterally, in which case it does not collect the tears properly. When the punctum is displaced forward, he cauterizes carefully behind it at repeated intervals until its position is nearly normal. Most of the time he uses a copper stick for this cauterization. He feels that excision of a small piece of tissue from the tarsal conjunctiva is sometimes indicated. When the punctum is displaced backward and opens into the tarsal conjunctiva, he pulls it forward by excising a fold of skin about 1 mm. wide in front of the punctum. He takes out a wedge-shaped piece of skin, with the wedge toward the top of the palpebral margin. When there is a lateral displacement of the punctum, it is more difficult for the passage of tears, since here the lake does not form in the conjunctiva so that tears can flow into the canaliculus. These laterally placed puncta should, therefore, be corrected. The affected lids have a tendency to peak at the punctum. The highest part of the lid is excised, so that the punctum then becomes the highest part of the lid margin. A number of combinations of these three groups of cases have been described. The commonest combination is a forward and lateral displacement of the punctum. He discusses many other anomalies of the punctum and complete absence of the canaliculus, and states that there may be two canaliculi in one lower lid, both of which usually end blindly.

The controversy of conservative treatment *vs.* probing of the nasolacrimal duct continues.* Hopkins[2] states that there are several causes of tearing in the newborn and thinks that conjunctival smears and cultures should be done on infants' eyes in order to establish a diagnosis. This is particularly true when there is any pus present during the first two weeks of life. Many cases of blocked nasolacrimal duct, he says, can be relieved by simple massage of the lacrimal sac; however, probing is many times necessary. He treats the condition conservatively, irrigating the sac with penicillin and giving penicillin systemically while there is pus in the sac.

Cassady,[3] on the other hand, advocates early probing instead of prolonged massage. He uses a No. 23-gauge straight 1 in. cannula attached to a 2 cc. syringe, which is filled with saline. This straight cannula is inserted into the punctum and the sac washed. If there is any obstruction, the cannula is used as a probe and ruptures through the membrane at the lower end of the duct by the usual maneuvers. In adults, one should take considerable time before starting a vigorous campaign on eyes with excessive

Received for publication Sept. 26, 1955.

* References 2 to 4.

watering. One must always be sure that there is an obstruction of the nasolacrimal duct. Cassady states that obstruction of the nasolacrimal duct is four to five times as frequent in women as in men. He usually probes the ducts first, even in adults. When probing is not successful, he does a dacryocystorhinostomy of the Dupuy-Dutemps type. In his experience dacryocystorhinostomy is successful in about half the patients; a quarter of the patients give fair results, and the other quarter give poor results or failures.

Hurd [4] reports on 26 cases, of which 2 were acute phlegmonous infections of the sac. In most of the patients tearing in the affected eye had been present since birth. In the two cases of acute phlegmonous infections tearing had been present since birth, and it was the author's opinion that the infection was started at birth. Of the 26 patients, 5 were cured by simple massage of the sac; 2 did not return, and 19 were subjected to probing, including the 2 with acute phlegmonous sacs, all of these responding without complication. All the five patients who responded to conservative therapy were under 5 months of age. The average age of the children examined was 5½ months. The youngest was 3 weeks and the oldest was 22 months. It is also interesting that Hurd [4] prefers to use the upper punctum for probing the nasolacrimal duct. Jeffery [9] states that it is important to wipe the mucus from the baby's eyes as the head emerges, as a means of prophylaxis against lacrimal-sac obstruction at birth. She had been taught many years ago that the simple wiping away of this mucus promptly would prevent sac trouble in babies later.

Chronic lacrimation and epiphora may present a considerable problem.† It is most important to determine whether the epiphora is caused by hypersecretion or is due to obstruction of the collecting apparatus. All possible causes of epiphora should be investigated before treatment is instituted. When the epiphora is due to an obstruction of the nasolacrimal apparatus, conjunctivitis is usually present, as is the case when there are concretions in the lacrimal canaliculi; as was pointed out by Mattsson,[5] a concretion in the upper canaliculus is frequently overlooked. There is considerable tearing with redness of the conjunctiva, particularly over the region of the inner canthus. The treatment is usually simple removal of the mycotic infection from the canaliculus.

Many times it is difficult in older people to find a definite cause for the epiphora. Herrenschwand [6] states that most ophthalmologists find some chronic conjunctivitis with epiphora and give the patient some form of drops, with no relief of symptoms. He states that usually there are senile changes in the punctum, which becomes rigid and can no longer pump or suck the tears from the conjunctiva. Splitting of the punctum may give some relief, particularly when there is a definite eversion of the punctum, but he feels that opening the punctum may give some relief for epiphora when there is no eversion. He states that one should attempt to bring back some of the old elasticity of the punctum. He uses 1% cortisone ointment to increase its elasticity. Thus he believes that, since cortisone is of value in other degenerating diseases, it will probably be of help in this simple disease.

When no cause can be found for chronic tearing, the Hubbards [7] recommend severing of the lacrimal ductules from the conjunctiva as they come from the lacrimal gland. The authors claim that this is an anatomical and physiological method of decreasing the tears. This can be done either with or without excision of a portion of the lacrimal gland, with very satisfactory results. Their operation is performed with local anesthesia in the office or in the hospital. The palpebral portion of the gland is easily isolated. They state that it is important to make the incision far enough laterally into the area of the external canthal ligament in order to get the large ductules that drain from that area. The incision is made from 1.5 to 2 cm. in length and extends medially just above the tarsal plate.

† References 5 to 8.

Chronic tearing may be decreased by treating the cause of the tearing, which may be conjunctivitis, an everted punctum, or any of the numerous other factors that may produce epiphora. I believe that these should be investigated thoroughly before any of the lacrimal ductules or the palpebral portion of the lacrimal gland is removed. When the epiphora is associated with Horner's syndrome, removal of part of the lacrimal gland certainly produces gratifying results. In my experience, many more people suffer from lack of tears than suffer from epiphora.

Familial autonomic dysfunction was discussed in the former reviews, and the question was considered whether congenital alacrima, or the absence of tears in children, is associated with this disease, as described by Riley and associates.[11] Dunnington[10] presents from the ophthalmological viewpoint three cases of congenital familial autonomic dysfunction with the typical findings. Riley and co-authors[11] present further observations on familial autonomic dysfunction, which he now terms "familial dysautonomia." Riley[11] has now collected a total of 48 cases of this disease in children. Only one child, the last case, which appears to be typical, is not of Jewish extraction. The facts about the family support the theory that this condition is of genetic origin. The disease or anomaly is probably transmitted by an autosomal recessive gene. Apparently, it is also significant that there is dwarfing in all these children. It is also significant that there is postural hypotension, in which the blood pressure drops when the patient stands in the erect position and may be normal or elevated when he is lying down. Many of the abnormalities are probably brought on by the parents, and the author presents a scheme for the development of the emotional disturbances due to overanxiety on the part of the parents. These children present many problems in treatment.

Radnót and Wallner[12] could find only 14 cases in the entire literature in which there was a congenital absence of tears. They say there may be more patients who have diminished lacrimal secretion. They present the case of a 6-year-old girl whose parents said that the child cried without tears. The authors state that at 2 years of age this child could eat solid food only by drinking water, since there was also lack of saliva. Both corneas, however, were clear. Lacrimation was found by the Schirmer test to be greatly decreased. The diminished salivation produced glossitis, with marked caries of the teeth and dryness of the skin. There were no other changes associated with this lack of salivation and absence of tears.

Sjögren's Syndrome

The treatment and diagnosis of Sjögren's disease continues to be a problem.‡ Some authors claim that corticotropin given intramuscularly is of some benefit, but its use is controversial. There is no doubt that it decreases the symptoms of the arthritis, but there is no evidence that there is an increase in salivation or in lacrimation while the patient is on the drug. The 17-ketosteroids in the urine are usually decreased in Sjögren's disease.

Some authors § feel that the sialogram of the parotid may be a useful tool in obtaining a roentgenologic examination of the glands. In this test a radiopaque substance or contrast medium is injected under pressure into Stensen's duct. When there is good filling of the ductule system, the parenchyma can be visualized. This gives an x-ray impression of parenchymal atrophy.

MacLean and Robinson[14] report finding L. E. cells in the peripheral circulation in patients with Sjögren's syndrome. In their patients these cells disappeared from the peripheral blood after cessation of hormonal therapy. L. E. (lupus erythematosus) cells are pyknotic cells which are apparently polymorphonuclears that have phagocytosed other polymorphocellular leucocytes and formed a nuclear mass.

The treatment of keratoconjunctivitis sicca has been a problem, but Rubin[16] claims that the use of egg white will relieve some of the symptoms. While many of us have

‡ References 13 and 14.

§ References 14 and 15.

sometimes used egg white as a collyrium in keratoconjunctivitis sicca, Rubin [16] has used it for about 15 years. He instructs the patient to beat the white of the egg into a froth and then store it in the refrigerator. The solution which forms from this frothy mixture is used as eye drops. When it must be used over a period of time, the fresh egg is prepared twice a week. Most of the patients claim improvement and are extremely grateful. It is well known that egg white contains large quantities of lysozyme. McEwen and Kimura [17] have shown that there is a decrease of lysozyme in the tears of patients with kerotoconjunctivitis sicca. They used a filter-paper electrophoretic method for protein analysis of a patient's tear fluid; one protein component moved to the negative pole at pH 7.8. This was identified as the lysozyme fraction because electrophoretically it was indistinguishable from the crystalline egg-white lysozyme and because of its activity toward Micrococcus lysodeikticus. Radnót and Németh [18] claim that testosterone preparations will increase lacrimal secretion in keratoconjunctivitis sicca. They justify these claims by experimentation on rabbits. With the injection of testosterone into female and castrated males, they showed increase in the weight of the lacrimal glands. Hyperactivity of the parenchyma of the gland could be demonstrated histologically.

Nover,‖ in a series of experiments on rabbits, tried to explain the functions of the lacrimal gland. He estimated the secretion of tears by Schirmer's method and with the fluorescein dilution test in normal animals, in rabbits after operation, and in treated animals. The tearing function in rabbits is slight and of minimal importance. After partial extirpation of the lacrimal gland in the normal rabbit no diminution in function is observed. After thyroxin was given intravenously, an increase in secretion was observed; however, after extirpation of the gland the thyroxin-treated animals did not show increased secretion. Transplantation of the lacrimal gland will produce some restoration of the function of the gland. He feels that from these experiments there is evidence that the thyroid hormones may be of value in treatment of Sjögren's disease. The lacrimal gland will also regenerate in rabbits, but he feels that the regeneration is faster if the rabbits are pretreated with thyroxin. He also placed the glandular material to be transplanted in a thyroxin solution for 10 minutes prior to transplantation under the skin of the upper lid. This pretreatment did not influence the regeneration. He therefore assumes that the thyroxin effect is a hematogenous rather than a local one.

‖ References 10 to 21.

Tumors

Tumors of the lacrimal gland continue to be a vexing problem. Forrest [22] tried to demonstrate that the benign and malignant variations of the lacrimal gland tumors can be distinguished histologically and, on this basis, proper treatment instituted. He reports on 26 specimens of epithelial tumors of the lacrimal gland. Some of these tumors are included as mixed tumors, while others are more aggressive in their behavior and may be referred to as carcinomas. There were 11 specimens which were called benign mixed tumors. These were encapsulated and contained cystic areas with serous or mucinous secretion. The specimens which were classified as true benign mixed tumors included tissue elements which ran the gamut from the solid cellular areas of epithelial cells and cords, including glandular areas, to connective tissue and cartilage. Ten specimens were classified as the adenocystic variety of carcinoma. Five specimens were of the miscellaneous type. Forrest's [22] cases presented many interesting clinical features. Some of the findings are as follows: Tearing is usually associated with the benign mixed tumor, while pain indicates an adenocystic type of carcinoma. Eight of the eleven patients with benign mixed tumors are living and well. Seven have survived an average of seven years. Two of these patients have survived 16 and 21 years, respectively. Six of the

patients with adenocystic carcinoma died an average of five years after the initial operation. Two of the patients are living with the disease. Among the remaining patients with carcinomas other than the adenocystic type, five died at an average of two and a half years after operation. Forrest [22] states that if the entire tumor is removed and a histological examination shows that it is a benign mixed tumor, nothing further should be done. If it is a malignant tumor, immediate further operation should be carried out. Everything should be removed. The roentgenologist may be of aid in determining the extent of the bone invasion, and, with the assistance of the neurosurgeon and the rhinological surgeon, an attempt is made to excise all of the involved bone. This may involve entrance into the cranial cavity and the sinuses. Exenteration of the orbit is essential, and no attempt should be made to preserve the lids. In the experience of Forrest [22] procrastination, aimed at preventing disfigurement, will not save the patient. The only hope is early and aggressive surgery. Radiation is limited to treatment of the adenocystic carcinomas, which, although radiosensitive, have not been proved radiocurable.

Jones and Pfeiffer [23] present a roentgenologic study on 20 patients with proved tumors of the lacrimal gland. The roentgenograms of 18 of the 20 patients showed changes associated with gland tumors. The two examinations that revealed nothing abnormal occurred in cases of slow-growing, benign mixed tumors, and it is probable that these may be of some significance. The high percentage of positive results in the remaining 18 patients compares favorably with that in the rest of the field of radiology. Four varieties of abnormalities were distinguishable on the films. The first is the presence of an enlarged lacrimal fossa on the involved side. The bone cortex is intact, but the fossa becomes enlarged. The second is the presence of increased density of the bone adjacent to the lacrimal gland. The third feature is a combination of an enlargement and an increase in density. The fourth abnormal feature is erosion of the bone. Jones and Pfeiffer [23] wish to emphasize that an opportunity lies within the grasp of the ophthalmologist to benefit from all the roentgenograms in early and repeated visualization of the lacrimal gland tumors as a prognostic sign.

Arnold [24] reports a most interesting tumor of the lacrimal gland. It produced unilateral exophthalmos of the right eye. She states that the right eye had always been somewhat prominent but had increased considerably in the last few weeks, associated with pain, swelling, and diplopia. The orbit was explored through a brow incision and a fluctuant mass found about the size of an English walnut. The cyst was adherent to the superior orbital wall and was ruptured on removal. The cyst was lined with flat, cuboidal, and pseudostratified epithelium. There was no evidence of a tumor. The diagnosis of an epithelial inclusion cyst of the lacrimal gland was made.

Operative Procedures

Dacryocystorhinostomy continues to be the surgical method of choice in repair of patients with chronic dacryocystitis and complete occlusion of the nasolacrimal duct.¶ Romanes [26] reports on 50 cases of the Dupuy-Dutemps operation. The results are taken in sequence and are unselected. The authors determined the postoperative results by injection of iodized oil U. S. P. (Lipiodol). An obstruction of the sac was found in 19 cases; 13 of the patients were cured; 4 were unimproved, and the results for 2 were uncertain. When the site of block of the nasolacrimal apparatus was in the duct, 26 of the 31 patients operated on were cured, 1 was unimproved, and the results for 4 were uncertain. A cure was obtained in 90% of the patients operated on. During the Dupuy-Dutemps operation most of the patients had a rubber catheter inserted similar to that reported by Iliff.[28] Iliff [28] inserts a No. 10 or No. 12 ureteral catheter, which is passed through the trephine opening into the nose and out the external naris. The upper end of the

¶ References 25 to 28.

catheter is sutured into the lacrimal sac. Milder [27] prefers to use dacryocystograms as an aid in the preoperative and postoperative treatment of the obstructions of the nasolacrimal duct.

Hefel [28] reports the results of 74 operations of the Dupuy-Dutemps type. These 74 operations were performed upon 65 patients. Successful dacryocystorhinostomies were performed on 87%. In the remaining patients a simple dacryocystectomy was performed, with a permanent cure in eight.

Mahlen [29] presents a case in which the removal of the sac was followed by the development of a granuloma. Examination of the granuloma after it was removed showed that the granuloma contained talcum crystals. The demonstration of the talcum crystals was done by the polarized microscope. Tuberculosis of the lacrimal sac occasionally is found; however, Hallermann [30] reports a case of pseudotuberculosis of the lacrimal sac in which the examination with polarized light revealed a doubly refractile substance, consiting of particles of powder. These crystals were thought to be one of the sulfonamides that had been used as a powder to dress open wounds. It produced epithelioid cells and giant cells histologically similar to those found in tuberculosis of the tear sac.

Jones [31] has devised some interesting surgical procedures in discussing ways of connecting the canaliculus through the sac into the nose. He has made a new canaliculus by using a portion of the sac to put over polyethylene tubing. From my experience, I have found that the conjunctival dacryocystorhinostomy works better in this procedure. Jones has also performed a number of conjunctival dacryocystorhinostomies, with apparently good results. In one procedure he makes a pedicle-type flap from the mucous membrane of the nose; this is used to line the ostium that extends into the nose. I have successfully transplanted the canaliculus into the conjunctiva when there is a stenosis of the canaliculus. Jones describes a procedure similar to this but sutures the fundus of the sac to the conjunctiva.

THE EYELIDS

Anomalies

Congenital anomalies of the lids are comparatively rare. Ptosis or blepharoptosis is one of the commoner congenital anomalies. Fisher and his co-workers [32] found an inherited combination of purpura simplex and ptosis in four generations of one family. The purpura was classified by an evaluation of the hematological study. The name "hereditary familial" purpura simplex had been given by Davis. The combination of blood dyscrasia and ptosis was found in 8 of 13 persons examined. In most of the members the ptosis was bilateral; however, in one the ptosis was unilateral.

Berke and Wadsworth [33] attempted to evaluate histologically the levator muscle in congenital and in acquired ptosis. In this excellent article, 84 biopsy specimens are studied. These specimens, which were removed at the time of resection of the levator, were all long enough to include all of Müller's muscle and some of the striated muscle fibers of the levator. Abundant normal-appearing striated muscle fibers were always found in all cases of acquired ptosis. In congenital third-nerve paralysis and in patients with the jaw-winking phenomenon, striated muscles were found. In congenital ptosis striated muscles were always sparse or absent, so that if the ptosis measured only 2 mm., only a few striated muscles were present. If the ptosis measured 4 mm. or more, the striated muscle fibers were always absent; but if the ptosis measured exactly 3 mm., about half the cases showed some muscle fibers and half did not. The absence of striated muscle fibers in all cases of acquired ptosis of more than 3 mm. would tend to indicate that the amount of ptosis in the given case depends upon the number of striated muscle fibers present. Müller's upper lid muscle was always present, even in acquired or congenital ptosis. The presence of striated muscle in the acquired cases does not insure a high percentage of postoperative results; however, the number of striated muscle fibers present in congenital ptosis seems to be an important factor in determining the final results. A higher per-

centage of satisfactory results occurred in those cases in which a large number of striated muscle fibers were present, and the unsatisfactory results were obtained where the striated fibers were absent. From these histological studies, the authors conclude that congenital ptosis is primarily a defective structural development of the levator muscle. The methods of correction of blepharoptosis have been discussed in the previous reviews.

Johnson [84] reports on the results of 162 operations. He emphasizes that if Bell's phenomenon is not present, there is some danger of the postoperative development of exposure keratitis. He feels that any strabismus should be corrected before one proceeds with the ptosis operation. If blepharophimosis is present, it should be corrected either before or at the time of the ptosis surgery. While Berke [33] measures the amount of ptosis, Johnson [84] feels that the measurement of the ptosis does not give a good indication of levator function. He records the amount that the upper lid overlaps the cornea in the primary position. He emphasizes that the presence of the lid fold, which deepens on upward gaze, indicates that the levator fibers are present and attached to the skin and have, at least, some potential function. This is a strong indication that a resection of the levator muscle should be desirable. Operation should be postponed until some cooperation on the part of the patient can be obtained, unless the case is one of bilateral ptosis that is so bad that the patient must hold the head far back in order to see under the lid. In the last instance, one should operate before the child begins to walk. When ptosis is unilateral, one should operate before amblyopia becomes irreversible; otherwise, one should wait until the age of 3 or 4 years. Johnson [84] warns of the danger of exposure keratitis as an immediate postoperative result when the superior rectus has been used in place of the levator, as in the case of the Dickey, the Motais-Parinaud, and Berke's [33] modification of the Motais operation. The Blaskovicz operation has the widest application. Since there is very little postoperative reaction, lagophthalmos is rare, and the lid moves better with the globe. The dangers of postoperative diplopia are also decreased. Johnson states that good results can be obtained by resection of the levator even with third-nerve paralysis or congenital paralysis of upward gaze. Contrary to most authors, he prefers the resection of the levator in the Marcus Gunn, or jaw-winking, phenomenon. In the 162 cases of ptosis, the poorest results were obtained after resection of the levator in eyes with a weak superior rectus and the best results after resection of the levator in eyes with no other muscle anomalies. In the former group the proportion of good results was 56%, and in the latter group, 85%.

McEvitt [85] presents a new procedure similar to the use of a fascia lata sling for the frontalis muscle. This procedure is particularly adaptable in cases of paralysis of the levator. He uses a sheet of fascia lata which is roughly keystone-shaped. The wide end of the keystone is fastened at the lid border, and the small end is inserted in the frontalis; an incision, 1.5 cm. in length, is made in the upper margin of the eyebrow. Another incision, of the same length, is made a few millimeters behind the margin of the eyelid. The tissue between these incisions is undermined. The fascia lata sheet is then inserted, with the wide end down, and is sutured to the eyelids. The fascia lata is then made tense and sutured fairly deep, through the orbicularis muscle. It is then sutured to the frontalis muscle. The suturing of the fascia lata through the orbicularis near the upper edge of the tarsus is important in preventing the eyelid from pulling away from the eyeball. The authors claim a more uniform curve of the upper lid by this method.

Lasky [86] describes a rare anomaly in which there was an adhesion between the upper and the lower lids that had been present at birth. This he called ankyloblepharon filiforme adnatum. The adhesion ran from the gray line in the lower lid to the gray line in the upper lid, and the cilia were free from any involvement. Simple severing was all that was necessary to effect a complete cure. This is apparently only the 2d case reported

in the English literature and the 13th case in the world literature. While I have never seen a case, our plastic surgeon reported that he had recently cut adhesions between the eyelids while doing a harelip operation.

Swan [37] presented an interesting syndrome of congenital epiblepharon, epicanthus, and insufficiency of the inferior oblique. The epiblepharon may be caused by a fold in the inferior palpebral fold. This causes an infolding of the cilia of the lower lid, so that at times the lashes will scratch the cornea and produce keratitis. The epiblepharon and the epicanthus usually disappear with growth. However, when the cornea was scratched, Swan [37] performed surgery and found a hypertrophic bank of orbicularis fibers along the nasal half of the lid margin, which he excised. While Swan [37] emphasizes that insufficiency of the inferior oblique is part of the syndrome, I have seen a number of fat infants with epiblepharon who had no demonstrable insufficiency of the inferior oblique.

Acquired ptosis of the upper lid may be the earliest sign of myasthenia. # In a review of 42 cases of myasthenia, the earliest changes occurred in the eyelids. Ocular muscle weakness was found in 24 cases. The resistance to opening of the eyelids is presented as a diagnostic test. This test is usually positive in all the patients, even though there are no ocular symptoms. The attempt to open the eye forcefully usually disappears after an injection of neostigmine.

Jacobs [40] devised an instrument for measuring the strength of the orbicularis muscle. The instrument consists of a piston and a cylinder connecting a pair of lid specula, which are introduced into the palpebral fissure. The specula are forced together by the power of the patient's lids closing. The air pressure thus produced is read on a mercury manometer. The instrument is calibrated against weight. An effort was made to determine the normal value of the strength of the orbicularis muscle. The average of many medical students was between 120 and 140 mm. of mercury, with a wide range above and below that figure. Male subjects were found to be slightly stronger than female. Although Jacobs [40] had trouble in finding a definite base line, this instrument may be applicable in cases of myasthenia gravis or in other cases in which there is weakness of the orbicularis and drugs can be used to determine the course of recovery.

Fabing [41] presents a reasonably new treatment for severe blepharospasm—a new cerebral stimulant α-(2-piperidyl)-benzhydrol hydrochloride, which is sold under the tradename of Meratran by the Wm. S. Merrell Company. The authors used the material to treat three cases of severe blepharospasm, with gratifying results. Five milligrams given three times a day produced marked improvement. When the dose was increased to 20 mg. a day, the patients were uncomfortably alert and their sleep was interrupted. A dose of about 5 mg. a day seems to be the best amount, although no conclusions can be drawn from the small number of cases. It is encouraging to continue the study of this drug. I have treated one patient, with good results.

An ingenious study on the development of the elastic fibers was carried out by Higuti.[42] He cut the nerves to the nictitating membrane on one side in tadpoles and followed the development of elastic fibers in this membrane. Elastic fibers did not develop on the side on which the nerves were removed, while they were present on the normal side. It was concluded that the development of elastic fibrils depends upon the movement of connective tissue stroma, in which elastic fibers will be found.

The surgical repair of entropion and ectropion is usually based on standard principles of operations already described. Each of these operations requires individual variations to fit the patient and the surgeon.* These surgical procedures may be extremely simple, such as the correction of the senile entropion by Butler.[43] He removes a triangular piece of tarsus from the outer third approximately 3 mm. in length, with the base of the triangle away from the line of cilia.

References 38 and 39.

* References 43 to 53.

This area of tarsus is removed and closed with black sutures. At times he removes an elliptical piece of skin from the temporal side of the lower lid in order to help in correcting the entropion. The entropion produced by trachoma [54] must be repaired by other methods. Tarsectomy or excision of the conjunctiva, with replacement by mucous membrane from the mouth, may be necessary. Total removal of all of the orbicularis fibers has also been used. There are also operations that are similar to the Hess suture for ptosis, in an effort to turn out the lower lid, particularly in cicatricial entropions.

Wies [52] describes a type of operation for senile or spastic entropion in which he cuts through the entire thickness of the lid about 3 mm. below the free border. This incision extends through skin, orbicularis, and tarsus and into the conjunctiva. Three double-armed sutures are then placed in the lower lip of the conjunctiva and brought out through the incision in the lower border of the skin. The skin is then closed. Some authors, in treating ectropion, prefer to use full-thickness free skin grafts, while others prefer pedicles.

Cole [46] has devised an interesting operation in which the tarsus is split from the skin of the upper lid and implanted into the lower lid. He has also reversed the procedure and sutured the eye closed. After a healing time the eye is opened at the palpebral fissure and a satisfactory cosmetic result obtained.

Groenvall [47] reports that he uses two pedicle flaps, one from the upper lid and the other from the temporal side in which the skin is advanced from the forehead. Repair of the upper lid is usually more of a problem than repair of the lower lid because of the mobility of the upper lid.[49] The function of opening and closing the eyelid must be constantly borne in mind. Operations have been devised in which large sliding flaps are taken from the zygomatic and temporal regions. The conjunctival lining may be brought down from excesses of the superior fornix.

Callahan's [53] three composite lid grafts may also be useful. It is interesting that most authors have difficulty in obtaining eyelash grafts, particularly those that will look like eyelashes. Beard [49] appeals that either a tattooed pigment line or paste-on lashes be used, instead of the attempt to grow eyelashes. Reconstructive surgery of the eyelids requires ingenuity and careful review of all surgical procedures before any attempt is made at repair in an individual case. One should be well versed in all forms of free grafting of skin, as well as of mucous membrane.

Klemens [55] points out that tarsorrhaphy may be helpful in cases of ectropion, but a tarsorrhaphy may evert the puncta or it may interfere with vision. He devises a new procedure in which the tarsorrphaphy is done nasal to the puncta and the skin is mobilized over the canaliculus very close to the puncta. Another vertical incision is made near the medial canthus and a rectangular flap is prepared. The two flaps are brought together with a mattress suture. This procedure shortens and narrows the inner canthus when an ectropion has been present for a long time.

Gifford [56] feels that the rough, irregular mass of tissue that proliferates on the conjunctival surface of the lid cannot safely be allowed to impinge upon the cornea. He removes the entire mass and the underlying tarsus. If the removal of the mass does not correct the ectropion, a small Kuhnt operation then completes the procedure. Gifford [56] says that not more than 5 mm. of tarsus should be removed from the upper tarsus.

Sayoc [57] has devised an operation to form a skin fold to improve the appearance of persons born without a fold in their upper eyelids. An incision is made through the skin of the upper lid in approximately the area where the normal lid fold should be. This incision is carried through the subcutaneous tissue down to the tarsus. A narrow strip of orbicularis, from 1 to 2 mm. in width, extending from the nasal to the temporal end of the incision, is excised. This exposes the tarsus, to which the skin is to be sutured. Absorbable surgical sutures U. S. P. are used to fasten the skin to the exposed tarsus. The skin is then closed. A similar proce-

dure [58] may be used to correct redundancy and looseness of the skin of the upper lid; this produces a fold extending over the free border of the lid and may interfere with vision. A simple excision of a crescentic piece of skin may be sufficient to relieve this redundancy. When the prolapsed fat is present, some removal of fat may be necessary, and if the redundancy is severe, the skin may have to be attached to the tarsus.

Inflammatory Diseases

An interesting study was carried out by Roodyn [59] on staphylococcal infections. In all cases of boils and styes, nose cultures were taken at the same time. There were 71 patients with boils and 22 patients with styes. Identical strains of staphylococci were found in the boil or stye and in the nose in 77%. Only 5, or 23%, did not have nasal staphylococci. About one-fourth of the 22 cases of staphylococci cultured from styes were resistant to penicillin, while 30% of those from the nose were penicillin-resistant. While most typing methods of staphylococci are not reliable, the author used a bacteriophage method of typing, which he states is the most reliable. In his investigation it was possible to discover nine families in which there was a spread of single-phage type of Staphylococcus from one person to another within the household. The immediate infectivity of a boil or style appears to be low, and the author feels that many of these reinfections occur from the nose. He states that there is a high nasal carrier rate of staphylococci occurring in the nose of normal people. The eyelids, the arms, the face, and the nose are the commonest sites for boils. He was able to isolate 113 strains of staphylococci obtained from pus. Of these, 85% could be phage-typed. When recurrences of boils or styes occur, the reappearance of the original phage pattern of staphylococci is apparent. The infection is not a fresh one from a different strain. Most of the recurrences occurred in from 1 to 24 months.

Selsun (selenium sulfide) seems to be a safe material to use in the treatment of blepharitis marginalis and seborrheic blepharitis.† Bahn [60] divides the treatment into that of the lid and that of the scalp. He applies a suspension of selenium sulfide after nonalcoholic shampoos of the scalp. The selenium sulfide must be washed out but may remain in contact with the scalp for 45 to 60 minutes. The treatment of the meibomianitis and blepharitis consists of expression of the glands, and the lids are scrubbed with selenium sulfide ointment. He stresses the need to impress the patient that treatment should be continued even though the symptoms are relieved in a short time. This is to prevent relapses. He reports 100 cases of moderate, severe, and mild seborrheic blepharitis. Of these, 80% were asymptomatically and clinically clean at the end of the second week of treatment. He was able to obtain relief of symptoms by the end of the third week in 92% and in 97% at the end of the fourth week. There were recurrences in eight patients.

Cohen [61] treated 40 cases of blepharitis marginalis with selenium sulfide; 37 were improved, and there was 3 failures, 2 in cooperative patients and 1 in a patient who stopped using the treatment because of burning of her eye. In my experience some forms of selenium sulfide produce local irritation in the conjunctiva.

Theodore ‡ has continued his interest in allergies of the eyelids and presents a differential diagnosis of the eczemas of the lids. He divides them into the allergic eczematoid dermatitis, the infectious eczematoid staphylococcal dermatitis, and the generalized dermatoses, such as atopic dermatitis, neurodermatitis, seborrheic dermatitis, and psoriasis. The commonest allergic form is that which occurs on the lid border. Cosmetics and ophthalmic drugs account for most of the contact allergies. Less often, articles of apparel, such as jewelry, metal plastics, and other chemicals or animal and vegetable products may produce a reaction. Recently, some of the common ingredients used as insect repellents and depilatories have pro-

† References 60 and 61.

‡ References 62 and 63.

duced a contact eczematoid dermatitis. The reactive substances that produce contact dermatitis may be divided into two classes: the primary irritants and the mucosal and cutaneous sensitizers. Unlike an allergen, the irritant may produce or develop symptoms the first time the substance is used, whereas, in contrast to this, the sensitizers must act as true allergens and take time for their development. Most of the ophthalmic drugs are true sensitizers when the conjunctiva is the point of contact. The allergic reaction begins in the conjunctiva but involves the adjacent skin, such as a typical dermatitis from atropine. While Theodore [62] has described some of these changes before, one must always think of the presence of an irritant in addition to the allergen. All the cosmetics or beauty aids may produce eczema of the eyelids. He states that of all the ocular allergies that can be traced to cosmetics, those due to nail polish and nail lacquer are by far the commonest. When there had been dermatitis due to nail polish or nail lacquer, 78 of 100 cases had some involvement of the eyelids. When there is a sensitivity to lipstick, it is usually due to an indelible dye. Theodore [62] discusses at length the development of the eczematoid staphylococcal dermatitis, which he believes, with Thygeson, is due to the direct action of the toxin of the Staphylococcus on the skin. His concept of the mechanism of staphylococcal eczema is well presented. He believes that the direct contact of the staphylococcal toxin plus an allergic reaction produces the inflammation. Staphylococcal polysaccharide may produce an immediate reaction, or there may be a delayed reaction. He stresses the use of antibiotic agents and vaccines in the treatment of staphylococcal conjunctivitis and blepharitis. In all types of eczema of the eyelid care must be exercised in their treatment, and one should proceed slowly. Sometimes an astringent, in the form of wet dressings, is indicated. Camomile tea or cold milk is the mildest astringent. He discusses many other forms of treatment. The therapy will usually vary according to the cause of the condition. The correct diagnosis is most important in order to carry out good treatment. In the discussion of Theodore's [62] paper, Thygeson suggests that all ophthalmologists should study it thoroughly because it contains considerable useful information.

Herpes Zoster Ophthalmicus

Cope and Jones [64] state that there are four types of herpes zoster. The commonest is that involving the lower neuron; however, the lower motor neuron may also be involved. Another type is a myelitis; the third is an encephalitis, and the fourth, the rarest type, in which a hemiplegia occurs in the absence of other signs of encephalitis. The authors were able to find only three cases previously reported. They present the case of a 54-year-old woman who gave a history of having had herpes zoster in the thoracic region some 20 years previously. Approximately five weeks before admission she developed herpes zoster of the ophthalmic division of the right fifth cranial nerve. On her admission to the hospital there was rather extensive rash over the distribution of this nerve and the patient had considerable pain. She developed partial left hemiplegia with difficulty in speech. The right side of her body was entirely normal. There was no rigidity of the neck, and Kernig's sign was negative. The authors postulate that the hemiplegia was due to the virus having spread from the trigeminal region. After a latent period of three weeks, the virus invaded the adjacent portion of the brain, attacking the pyramidal track and causing the hemiplegia. I have wondered whether the hemiplegia could have been an incidental vascular accident.

Miscellaneous Conditions

Emphysema of the eyelids is usually caused by a fracture through the ethmoid sinuses, in which air is blown through the sinuses into the loose lid tissue. Schenk,[65] however, reports a very unusual case. A 65-year-old man had a rather severe injury while inebriated. He fell heavily against a stone with his right thorax, cracked several ribs, and injured his lungs. A generalized

emphysema of the skin of the thorax developed, which later extended under the skin of the face and into the eyelids.

Pubic lice involving the eyelashes are apparently commoner in India than they are in the United States. Bose [66] reports that pubic lice occur mostly in the eyelashes of children and produce a moderately severe blepharitis. Bose [66] also states that on occasion the pubic lice will infest some areas of the scalp. In my experience, body lice are rare on the eyelashes, but pubic lice do occasionally occur. Most of those that I have seen have been in middle-aged women. The condition is certainly rare in children. Bose [66] says that pyrethrum in petrolatum U. S. P. (vaseline) 1:8 concentration may be used for five consecutive nights. While pyrethrum has no effect on the eggs, it does destroy the adults and the larval stages of the lice.

Tumors

The diagnosis and treatment of tumors of the eyelids remain about the same from year to year. The controversy between those who prefer surgical treatment and those who prefer radiation continues. A few unusual reports are found. Another benign calcified epithelioma was reported during the past year,[67] and this tumor may be commoner than has previously been suspected. Another benign epithelial neoplasm that looks like an epithelioma of the eyelid is called keratoacanthoma by Christensen and Fitzpatrick.[68] This rapidly growing tumor is clinically similar to a lesion of molluscum contagiosum. Simple surgical removal is all that is necessary for this tumor. A most unusual tumor was reported by Brockhurst.[69] The growth apparently originated in the mucous membrane of the maxillary antrum, which had been displaced to the orbital marginal region at the time of a previous injury to the floor of the orbit. A Caldwell-Luc procedure was done, and several weeks later the patient noted a mass, which began to increase in size. In the left lower lid was a mass, 3 by 30 mm. in size, involving the lateral two-thirds of the lid. It was of artgum consistency and was attached to the lateral portion of the inferior orbital margin. It proved to be a mucocele of the eyelid.

The eyelids are a favorite place for syringoma or multiple benign cystic epithelioma, according to Gaul.[70] He obtained biopsy material from 14 cases. No inheritance was demonstrated. The lower lid is the favorite site, but both lids may be involved. As a rule the tumors are bilateral. They make their appearance sometime after puberty. Most persons do not know they have them. A favorite location is the lid margin, especially the area of the lower punctum. One sees these tumors frequently. They are usually multiple, flat, and slightly white in color. They were first pointed out to me by Dr. Rubin Nomland, of our department of dermatology.

An unusually large plexiform neurofibroma was found in the left upper lid by Sabri and Diab.[71] This tumor was associated with café au lait spots and patches on the trunk and extremities. The orbit was also extremely enlarged. The authors state that 25 similar cases have been reported.

In discussing the surgical *vs.* the radiation treatment of tumors of the eyelids, Lockhart [72] stresses the surgical removal. He states that dermoids and cysts of the eyelids are common and may lend themselves to primary removal with surgery. Xanthelasma he also removes surgically. When a hemangioma or a port-wine stain appears in the eyelid, and if it is not too large, it may also be removed surgically. He feels, however, that the strawberry nevus in infants should be left alone. If treatment seems to be indicated, however, surgical removal is the simplest way. He also stated that some of the strawberry nevi could be reduced by exposure to light. In his series, 30 were basal-cell carcinomas; 4 were epithelioid carcinomas; 1 was a basosquamous-cell carcinoma; 1, a malignant melanoma, and 1, a lymphosarcoma. In only one instance was there a local recurrence after surgical removal, and this tumor was reexcised 15 months later. He uses free skin grafts, full-thickness sliding grafts, and primary closure in the repair of the surgical removal of tumors of the eyelids.

Birkner and Trautmann,[73] on the other hand, use contact radiation for most of their neoplasms. This radiation is from a 60-kv. machine, and he employs 0.15 mm. Cu for filter. Half the effective dose is reached within 1 cm. of the depth. This type of radiation is used in most cases of tumors near the skin. When the tumor is larger and more extensive, he gives deep x-ray therapy, in which he employs a 180-kv. x-ray apparatus. He prefers the low-voltage contact radiation therapy to radium because the dose can be better controlled. The size of the area can also be carefully controlled. He reports 85 cases of epitheliomas of the lids either treated or in the process of being treated. Fifty-three patients were observed for more than four years. Of these, 36 were cured after the first series of treatments; 17 required more than one series, and 3 died with metastasis. There was only one case in which an ectropion developed. No corneal changes were found. While conjunctivitis is sometimes present, it is comparatively mild. The authors do not believe that with x-rays of so low a voltage the bones can be damaged.

A recent study of xanthelasma was conducted by Robinson.§ He examined 568 elderly institutionalized patients to determine the incidence of this lesion. Of the non-Jews examined, 4% had one or more plaques, while 17.4% of the Jews were affected. The incidence of diabetes mellitus in this group of Jews and that for the non-Jews were about the same. None of the diabetic non-Jews in this study were affected with xanthelasma, while 44% of the diabetic Jews showed one or more xanthelasmic plaques. The average serum cholesterol level in the middle-aged and elderly non-Jews was 200 mg. per 100 cc.; however, the average for Jews of the same group was 300 mg. per 100 cc. There seems to be a significant elevation in the cholesterol levels in Jews with xanthelasma. This finding is not noted in non-Jews. Robinson[75] also treated 65 patients who had xanthelasma with cyanocobalamin U. S. P. Thirty patients were treated with oral cyanocobalamin, with poor results. Thirty-five patients were treated by parenteral administration of cyanocobalamin, with some beneficial results in 31. It is interesting to note that 10 patients were given 10γ; of these, 8 had good results, and 2 had poor results. Robinson[75] defined his good results as a definite diminution in the size of the plaque. He gave 15 patients 1000γ doses at weekly intervals. Fourteen had good results, and there was one failure. The results were classified as excellent in patients in whom there was a more marked diminution in the size of the plaque and complete involution of one or more of the smaller lesions. There was no change in the cholesterol metabolism during the use of cyanocobalamin. This series is comparatively small, and insufficient time has elapsed for possible recurrences to develop. Many ophthalmologists will be interested in trying this treatment.

§ References 74 and 75.

CONJUNCTIVA

Friedman[76] presents an interesting case of congenital symblepharon of the conjunctiva in the left eye of a 19-year-old sailor. Since there was no history of trauma or inflammatory disease, the condition was considered a congenital symblepharon or conjunctival fold.

Cases of calcium deposits and deposits of cystine ‖ continued to appear. Calcium deposits were found in the conjunctiva, cornea, and sclera in a case of acute parathyroid disease. Cystine in the cornea and conjunctiva was best demonstrated in biopsy material.[78] Chromatographic analysis of the dinitrophenyl derivatives of the amino acids present in the conjunctival material showed that the only low-molecular amino acid present was cystine. This substance was found in great abundance.

Bloch[79] has devised a special microscope for studying the conjunctival blood vessels of human beings. This microscope is equipped with a special photomicrographic camera, using a 45 mm. photographic objective lens, while the eye is illuminated with an oblique

‖ References 77 and 78.

strobe light. Bloch [79] describes aqueous veins and many of the normal vessels. While he does not draw any conclusions, he wishes to present the apparatus and to suggest its further use for study and photography of the vessels of the conjunctiva.

Passmore and King,[80] in a critical review of staining of the conjunctiva and cornea, attempt to explain the staining ability by chemical and physical means. The physical theory may account for the penetration of the dye into the tissue, while the chemical theory accounts for definite chemical affinities which the dyes have for certain tissues. The authors' primary interest, however, is in the staining of devitalized elements. They feel that fluorescein is still the most satisfactory stain for general use if sterility can be maintained. They are of the opinion that the use of polymyxin B sulfate in connection with fluorescein may prevent contamination by Pseudomonas aeruginosa. They feel that rose bengal is also valuable in diagnosis in early cases of keratitis sicca. Methylene blue seems to be an adequate vital stain for subepithelial tissues. Its action may be enhanced by prior use of cocaine, and counterstaining with fluorescein or scarlet red may be done for contrast. Vital staining of the conjunctiva has been of interest to many ophthalmologists, but Busacca [81] and Nataf [82] have discussed the lymphatics of the conjunctiva, which are brought out by vital staining. Nataf [82] described some of these lymphatics in 1953, but Busacca [81] says that he had already described these structures in 1948, when he injected trypan blue into the conjunctiva. Nataf [82] says that pirotrope blue is specific for the lypmphatic system. While Nataf [82] feels that pirotrope blue is specific, Busacca [81] says that the action of trypan blue is similar and stains the lymphatics. Busacca [81] shows pictures in which he states that the lymphatics are the same as those described by Nataf.[82] Nataf,[82] however, states that he continued Busacca's [81] investigation and pointed out recurrent lymphatic vessels that had not ben described by Busacca.[81] The photographs are convincing that lymphatics do occur in the conjunctiva, and I believe that they are not aqueous veins.

While rose bengal is not very widely used, many ophthalmologists employ this valuable staining material occasionally. It is used only occasionally because it is quite irritating when placed in the conjunctival sac. Sjögren has stressed that rose bengal should be used without an anesthetic. Many of us have felt that the prior use of an anesthetic was of little consequence. In an attempt to discover whether they would injure the cornea and conjunctival epithelium, Kronning [83] used two concentrations of five local anesthetics prior to the staining with rose bengal. The anesthetics and their concentrates were cocaine 4% and 8%, tetracaine 1% and 2%, Diocaine (*p*-diallyloxyethenyldiphenylamidine hydrochloride) 0.1% and 0.2%, procaine 2% and 4%, and lidocaine 1% and 2%. A 1% rose bengal solution was used to reveal the injury which might occur from the anesthetic. Each series of tests was performed on two groups, in order to investigate the drying effect of air on the development and intensity of the injury. The test showed that in human eyes the local anesthetic employed produced epithelial injury to the cornea and conjunctiva; with rose bengal staining a larger percentage of these injuries closely resembled keratoconjunctivitis sicca. The drying effect of air was found to have less significance than was formerly believed; however, the tests left no doubt that drying by air was an unfavorable effect. The results of these injuries were not serious, and healing as a rule took place in about three hours. No permanent injuries were observed in these tests. Forster [84] states that the preliminary use of tetracaine (Pontocaine) does not produce false-positive results in rose bengal tests. He states that Kronning [83] used the anesthetic solution three times at one-minute intervals prior to the instillation of rose bengal and did not remove the excessive dye. Therefore, he obtained more false-positive reactions. Forster [84] uses 1 drop of 0.5% or 1% tetracaine, which is adequate for surface anesthesia. The 1% rose bengal solution is allowed to stay

on only 15 seconds, and the excessive dye is removed by irrigation. He says that preliminary surface anesthesia does not destroy the value of the test but renders it a painless procedure and should be used prior to the use of 1% rose bengal solution. Kronning [85] says that the instillation of rose bengal solution is a somewhat painful procedure if a pronounced keratoconjunctivitis sicca is present; however, in slight cases or in sound eyes it is not painful at all and the surface anesthesia is not necessary.

The conjunctiva has been accessible to various testing means and has been used to determine hypersensitivities to substances such as tuberculin and pollens. The use of the conjunctiva has been largely discontinued because of certain severe reactions that have occurred. Franke [86] reopens this controversial use of the conjunctiva as a test of focal reactions. He reports that Remky, in 1950, used a weak (1:1/1000) solution of histamine, which he dropped into the conjunctiva in order to get a reaction in the conjunctival vessels. Remky concludes that if there is a focus of infection in the head area, there is a higher percentage of reaction from histamine dropped in the eyes of the patients. If the infection was not in the head area, the test was negative. He also states that in some cases in which the infection was on one side the eye on that side showed the reaction, while there was no reaction in the other side. Franke [86] checked many of these findings. He did the conjunctival tests on 908 patients; of these, 268 patients were considered to be without focal infections; 38.1%, however, showed a positive reaction. Of the 432 patients with a focal reaction in the head area, positive conjunctival findings in the test were present in 57.6%. Among the patients with focal infection, he found 208 with foci of infection in the head and subjective symptoms. A positive test from the conjunctiva was increased to 67.6%. Franke [86] concludes that, while there certainly was a trend toward the histamine reaction in the conjunctiva with foci of infection in the head area, it was of insufficient evidence to be of diagnostic significance.

Bacteriology

The bacteriology of the conjunctiva has greatly changed over the last 50 years. This fact is brought to our attention by Smith,[87] who, in his summary, says there has been a decrease in the frequency of isolation of both pathogenic and nonpathogenic organisms. He states that this may be partly due to the wide use of antibioitcs. There has, however, been an increase in the number of Gram-negative bacilli found in the eye; and, for that reason, Smith [87] stresses that prophylactic (preoperative) drops should contain an antibiotic effective against the Gram-negative groups. He gives as examples streptomycin or polymyxin B sulfate. Smith [87] took 4864 cultures of clean eyes, of which 49.4% were sterile. In a group which he calls dirty eyes, only 136 cultures, or 34.5%, were sterile. In a group of clean but previously antibiotic-treated eyes, 213, or 60%, were sterile. It is interesting to note that Smith [87] discovered a strain of Proteus vulgaris that was resistant to all therapy.

In a survey of 3000 patients in the Los Angeles area conducted by Soudakoff,[88] staphylococci, both pathogenic and nonpathogenic, were the commonest. He compares these findings with those in Europe and China, where the prevailing organism of acute conjunctivitis was the Morax-Axenfeld diplobacillus. Next in order after the Morax-Axenfeld organism was the Koch-Weeks bacillus (Hemophilus influenzae) and the Pneumococcus. In the Los Angeles area the Staphylococcus is commonest; however, the hemolytic Streptococcus and Corynebacterium xerose were next in frequency. It is interesting to note that of the 3000 cases pneumococci were found in only 18 cases and the Koch-Weeks bacillus in only 11 cases. He found that 21% of the cases examined by the laboratory showed no growth, while in the Freibury Clinic 31% grew no organisms and in the Chello Clinic, in China, 54% grew no organisms.

Since the Staphylococcus is one of the commonest organisms found not only in normal but also in inflamed conjunctiva, it is important to attempt to differentiate between

pathogenic and nonpathogenic staphylococci. Suie and Taylor [89] feel that the coagulase test is an aid in evaluating the potential pathogenicity of staphylococci. Staphylococci were isolated from 78 eyes with conjunctivitis, of which 51% were coagulase-positive. They were likewise isolated from 40 normal eyes, of which only 10% were coagulase-positive. It would be interesting to use the phage method of typing staphylococci, as reported by Roodyn.[89] Blender [90] discussed some of the commoner eye lesions seen by the family physician.

One of the most important features of examination of the external eye is the cytology of scrapings obtained from the conjunctiva. Kimura and Thygeson [91] state that the neutrophile reaction in the conjunctiva as presented by the scrapings stained with Giemsa stain is the most commonly encountered. It is most frequently associated with bacterial infections but is present in infections due to viruses of the Chlamydozoaceae (trachoma inclusion conjunctivitis and lymphogranuloma) and such fungous diseases as the Streptothrix concretion conjunctivitis. Erythema multiforme also is characterized by a polymorphonuclear cell exudate. In some of the vernal types of conjunctivitis, the neutrophile may be the commonest cell and is present in addition to the eosinophile. They also state that the neutrophiles are common in epidemic keratoconjunctivitis and herpes keratoconjunctivitis after the membrane has formed. They state that the eosinophile is the characteristic cell of allergic inflammation. They state that the eosinophiles are demonstrated in atropine sensitivity but absent in physostigmine or pilocarpine sensitivity. This suggests that the pilocarpine and physostigmine conjunctivitis is on a toxic, rather than on an allergic, basis. Occasionally, the basophile replaced the eosinophile in some patients. The mononuclear cells are commonest in the typical viral infections. In most diseases the small lymphocytes are prominent, but in some infections large lymphocytes may be present. The size of these lymphocytes is not of diagnostic significance. Plasma cells are sometimes found in scrapings from cases of trachoma. They may be found in other types of conjunctival disease, but their significance is certainly not known. Keratinization of the conjunctival epithelial cells is frequently associated with vitamin-A deficiency, exposure, scarring, keratoconjunctivitis sicca, and plaques in the epithelium. When the epithelium is keratinized and is associated with an overgrowth of C. xerose on the cells, the disease is most commonly a vitamin-A deficiency. Large multinucleated epithelial cells are more characteristic of viral than of bacterial infections. Pigment granules in the epithelial cells are apparently of no significance. Large and small pigment granules may aid in the diagnosis of conjunctival melanomas.

Allen [92] says that the cause of the infectious process of conjunctivitis should be determined and isolated in every case possible before therapy is started. Bacteria isolated from the conjunctiva should be used to determine the most effective therapeutic agent. The route of administration of the selected drug should be chosen on the basis of the clinical type of infection and the most effective therapeutic agent. An adequate dose of the therapeutic agent should be given, in order to maintain effective contact between the drug and the organism for a long enough period to eliminate the infection completely. Supplementary and palliative methods of treatment should be selected to promote the comfort of the patient without diminishing the effectiveness of the primary method of treatment. As aids to diagnosis, Allen [92] uses the Gram and the Giemsa stains, in addition to cultures, to determine the cause of infection. Mild superficial infections can usually be controlled by topical applications, but deeper and severer infections require oral or parenteral administration of the effective drug. Chronic and recurrent infections may also require immunization therapy. He states that neither cortisone nor corticotropin should be placed in the eye in the face of an acute infection, since the drug may actually increase the virulence of the infective agent.

Ophthalmia Neonatorum

Ormsby [93] reported on a study in Toronto, Canada, of ophthalmia neonatorum which extended from October, 1950, until September, 1954. In this study there were 8418 births. Gonorrheal conjunctivitis developed in 9 infants and inclusion conjunctivitis in 19. The cases were divided into four groups. Sulmefrin (sulfathiazole, sulfadiazine, and *dl*-methamphetamine) prophylaxis was used in 1703 infants, and there were 3 cases of gonorrheal ophthalmia and 7 cases of inclusion conjunctivitis. Ten per cent sulfanilamide ointment prophylaxis was used in 1570 infants. There were five cases of inclusion conjunctivitis and none due to the Gonococcus. One per cent silver nitrate prophylaxis was used in 3125 infants, and there were 4 cases of inclusion conjunctivitis and only 1 case due to the Gonococcus. In the final portion of the study, 2020 infants received no prophylaxis, and there were 5 cases of gonorrheal conjunctivitis and 3 cases of inclusion conjunctivitis. From this comparative prophylactic study regarding agents for ophthalmia neonatorum, it is obvious that gonorrheal conjunctivitis is infrequent. Ormsby says, however, that the use of 1% silver nitrate drops has stood the test of time, and this study has caused no harmful effect other than a mild chemical conjunctivitis during the first two postnatal days. While we await the outcome of present and future studies with antibiotics and chemotherapeutic agents, it is well to recognize that the Credé method is relatively harmless and is an effective prophylactic measure for gonorrheal ophthalmia in the newborn. No prophylaxis appears to be effective in prevention of inclusion conjunctivitis. Ormsby also reports that cases of staphylococcal infection occurred fairly commonly in the newborn. Smith and Halse [94] reviewed all of the gonorrheal infections of the eyes of newborn infants which were reported to the Public Health Service. In 1908 the rate of gonorrhea as a cause of blindness was 28%, and in 1950 it had dropped to 1%. They attribute this reduction to preventive medicine. It is interesting that only three states reported cases of gonorrheal ophthalmia in 1952, namely, Mississippi, South Carolina, and Tennessee. In view of Ormsby's [93] findings, I suspect that not all cases of gonorrheal ophthalmia have been reported.

Various Conjunctival Disorders

Gold, silver, lead, and mercury can all produce a chemical keratoconjunctivitis; however, the commonest cause of chemical conjunctivitis is H_2S gas.[95] Hydrogen sulfide produces an irritative type of conjunctivitis, which was discussed in last year's review.

Foreign bodies produce a severe conjunctivitis, particularly the grasses or the grains that contain sharp barbs. De Saint-Martin [96] reported an interesting foreign body under the lid of an 8-year-old boy who had played with the plant Hordeum murinum. A barb of this material was near the external canthus and projected approximately 3 mm. from the conjunctiva. It was difficult to remove the foreign body with forceps, with the use of local anesthesia, because of the sharp barblets, which immediately spread out on attempts to dislodge the body from the conjunctiva. The barb was approximately 2 cm. in length. Barbs from barley, wheat, and other grains occasionally become lodged in the conjunctiva and are sometimes very difficult to remove. De Saint-Martin [96] discusses the problem of differential diagnosis. If the head of a grain seed were to become completely buried in the conjunctiva, and not be visible externally, it would produce a rather severe conjunctivitis.

Bitot's spots have always been a problem, and Ascher [97] had an opportunity to study 22 patients with these spots. These patients were observed from a few days to 58 weeks during the winter of 1940-1941. Fourteen of the patients complained of pain, burning, and itching, and four complained of difficulty with close work and tired eyes; four had photophobia; three complained of watering of the eyes, and three had night blindness. The Bitot spots were unilateral in 17 of the 22 patients. In the remaining 12 patients

the spots were located on the temporal bulbar conjunctiva, and in 5, on the nasal conjunctiva. Of the 22 patients with Bitot spots, 45.8% had nicotinic-acid deficiencies. Riboflavin deficiency was present in 33.3%; thiamine deficiency, in 4.2%, and subclinical vitamin deficiency, in 16.7%. Bacteriologic examination showed C. xerose and epithelial cells in six of the eyes. Cultures from three of the eyes showed C. xerose, in one case associated with Staphylococcus aureus, in another with Staphylococcus albus, and in a third with Staphylococcus citrus. The xerotic spots simulated the foamy spots which are probably the forerunner of Bitot spots. No C. xerose could be found on the tarsal conjunctiva. A total of 60γ of riboflavin was given daily to two patients. The spots did not show any changes during or after treatment. No changes were observed in the spots with combined vitamin-B therapy. While the author feels that the Bitot spots are probably a vitamin-A deficiency, he feels that night blindness is a commoner and more consistent finding of vitamin-A deficiency. The night blindness disappears very quickly on administering vitamin A by mouth; however, the Bitot spots do not tend to change under this treatment.

The etiology of pterygium is still the subject of some controversy, although the inflammatory theory of Kamel [98] is gaining favor. He feels that the neoplastic theory should be dropped, since there are many facts against it. The degenerative theory has many backers, and various authors point to the fact that pinguecula is a precursor and consider that pterygium is a further step in the primary degenerative pathological process. There are almost always early signs of hyaline and elastic-tissue degeneration in the deeper parts of the pterygium. Pterygium frequently begins where a pinguecula is present. Kamel states that against the degenerative theory of pterygium there is a constant presence of round-cell infiltration in the cornea of early and progressive pterygium. There is also a marked increase in the goblet cells. Goblet cells increase with chronic inflammation and not with primary degeneration. He says that only chronic inflammation leads to damage and to disappearance of the superficial tissue, an overgrowth of a resistant connective tissue cell. Most of his points are in favor of an inflammatory origin, since the blood vessels are congested. Some pterygia disappear without leaving any trace; however, at times a pinguecula is left at the limbus where the pterygium disappear. Pterygia tend to increase in size and then stop.

In primary operations, Kamel [98] removes all the pterygium, doing a partial lamellar keratectomy over the part that includes the cornea. He cauterizes the undersurface with phenol. A small bare area in the sclera is left. He uses cortisone after the fifth day. He does very much the same thing for recurrent pterygium except that he dissects out all the fibrous tissue that overlies the sclera, in addition to doing a partial lamellar keratectomy. Many operations have been devised for pterygium, and most of them either remove the entire pterygium from the conjunctiva and cornea and resuture the wound, or leave the sclera bare. Some operators [99] make a keratome incision in the sclera and turn the head of the pterygium backward and bury it in the scleral wound. Fritz [100] presents a case of multiple pterygium associated with trichiasis and distichiasis. The pterygium may have been due to repeated attacks of phlyctenular keratoconjunctivitis. Three pterygia were transplanted upward according to the technique of McReynolds. There was little improvement in vision.

Purtscher [101] discusses a very interesting way of treating chronic irritations of the conjunctiva. There are many plants which can be mixed with water or buffered solutions that allow some of the material to get into the solution. Some of these are mucinous plants. When they are placed in water, they swell and form a collagenous solution. They are usually chemically indifferent but have a very high viscosity. These solutions combine with a mucinous portion of the precorneal film and protect the surface of the cornea and conjunctiva. This action prevents substances from going through this protective film. These solutions

decrease the itching and pain. A number of astringent solutions are made from plants, and they act as a mild acid. They precipitate the superficial protein and cause a slight shrinkage, similar to the action of alum. This causes a protective barrier and anemia of the conjunctiva, thereby decreasing the secretion and increasing the absorption. These substances are also slightly antiseptic. They attack micro-organisms by means of enzyme inhibition. They take away the conjunctival media on which the organisms grow. The mucinous plant material is used where there is not enough secretion, and the astringents are used where there is too much secretion, from the conjunctiva. The third group is the soapy plants. They produce an irritation of the conjunctiva and the adjacent glands. They produce hypersecretion of mucous substances and tears. They cause a burning pain in the eye, similar to that experienced when one gets soap in his eye. These plant drugs help the absorption of other drugs. The soapy solutions are used where there is insufficient mucous secretion and tears, as in keratitis sicca. The author presents a great many substances that can be used, such as pansies and flower leaves, the leaves of a birch tree, and many others. He has used most of these materials in his own eye, and if the solution burns too much he combines it with a drop of milk.

Theodore [102] has suggested that vernal conjunctivitis is a form of physical allergy to the warm season occurring in a person particularly predisposed. The warm season acts as a trigger mechanism to set off a sort of chain reaction, precipitating vernal catarrh under the proper conditions. Elimination of one factor may be all that is necessary to block the reaction and stop the process. He feels that the patient should be studied from the general point of view, taking all possible idiosyncracies under consideration.

Alimuddin [103] states that vernal conjunctivitis, like trachoma, is a disease of dirt and dust and is prevalent in tropical and subtropical regions. He states that about 31% of all ophthalmological cases seen during the summer have vernal conjunctivitis directly or superimposed upon trachoma, while in the winter about 1% of the patients have vernal conjunctivitis. The age group in which most of the cases occur is that between 10 and 20 years; this group accounts for 59% of the cases. The disease is rare after the age of 40. Of the 1871 cases which have been seen by the author, 1404 were in males and only 467 in females. He divides them into three clinical types: the palpebral variety, with pavement or cauliflower changes on the conjunctiva; the limbal variety, with vesicles and hypertrophy near the limbus (these two types occurring together in some cases), and an irritative type, in which there are very few changes in the conjunctiva. About 10% of the cases are of mixed type. Of the total number of cases, 579, or 31%, were of the irritative type; 523, or 29%, were of the limbal variety, and the rest were of the palpebral type. Associated allergies are frequently found, the commonest being skin allergies. Patches of discoid eczema, urticaria, contact dermatitis, or angioneurotic edema may be present. The author thinks that the less common associated features are manifestations of worm infestation, particularly hookworm, hay fever, and vasomotor rhinitis. About 30% of the irritative type become limbal within three years. None of the irritative variety have developed into the palpebral type.

Hydrocortisone seems to be more effective in the treatment of allergic conjunctivitis than does cortisone.[104] Hydrocortisone suspension could be instilled in the eyes at frequent intervals, from several times to twice a day. As soon as the symptoms are relieved, instillation of a maintenance dose of 1 drop of hydrocortisone suspension every few days should be followed. It may be necessary to combine the cortisone treatment with antihistaminic drugs taken by mouth at the same time in order to decrease the local hydrocortisone reaction. Although the authors treated only four patients and one patient obtained no relief, they feel that hydrocortisone is of therapeutic value.

Virus Diseases

Bietti [105] reviews the present status of virus research in ophthalmology. Since the publication of his book with Cavara, some further details have been brought out. He discusses the therapy of trachoma, which he feels is most effectively treated with sulfonamides; however, he also treats trachoma with benzathine penicillin G (Bicillin), which is a long-acting penicillin. He gives a total of 6,000,000 units of penicillin. He gives five intramuscular injections at two-week intervals. The penicillin treatment can be given for mass treatment. It is interesting to note that he concludes that cat scratch fever may belong to the lymphogranuloma-psittacosis-trachoma group of viruses, because there is cross agglutination found between patients with cat scratch fever and the lymphogranuloma-psittacosis group. In discussing herpes simplex virus, he states that the cauterization of the cornea is still the best treatment but that cortisone undoubtedly aggravates the condition. He mentions infectious mononucleosis and the conjunctivitis and choroiditis which sometimes occur with it. The Kopek spots in the conjunctiva in measles are frequently missed. He believes that epidemic keratoconjunctivitis is different from the nummularis keratitis of Dimmer. No results were obtained in his cases with any of the antibiotics. He feels that the Stevens-Johnson syndrome is probably on a virus basis but that there may be an allergic factor.

Trachoma

Trachoma is probably the most widespread virus disease. While it is uncommon in the United States, occasional cases do occur, and one should be constantly on the lookout for this disease. The volume of literature on trachoma is extensive.¶ Many of the publications have to do with prevention of trachoma, which is a major undertaking in many parts of the world. The prophylaxis of trachoma is effective provided treatment is carried out over a period of time and other infections are prevented. These mass treatments have largely been carried out in Morocco and Algiers. In most areas where trachoma is prevalent it is necessary to look for the patients, and not wait for their seeking treatment.[118] Many authors feel that education and the educational campaign against trachoma should continue. This educational program and case-finding program require the cooperation of ophthalmologists, school doctors, school nurses, teachers, and many public health personnel.[121] In Tunesia [122] efforts were made to prevent trachoma by also preventing acute conjunctivitis. Chlortetracycline (Aureomycin) drops were used two or three times a day for from 3 to 60 days. The school children were treated for 60 days, 10,958 being treated. In the general population, 181,079 were treated out of a population of 341,000. Tabulation of results for this enormous number of patients who were treated shows that their medication is very effective. Trachoma seems to be coming into France, having been brought there by colonial workers.[126] Patients often develop an abortive form of trachoma, which sometimes passes unnoticed when the examination is superficial. The disease may occur in children and will be manifested only by slight irritation of the conjunctiva. In children the lower fornix may be involved exclusively. The incipient pannus and inclusion bodies are helpful in diagnosis. Milder forms of trachoma seem to be much commoner now than before, particularly in Algiers, where along the seashore these abortive forms of trachoma are common and escape the recognition by the school authorities. More contaminations occur, therefore, since the cases go unnoticed. There is much more contagion in the schools than there is in the factories. The widespread use of eye make-up material may be a source of contamination with trachoma. In some cases the mode of contamination of the conjunctiva cannot be determined. Toulant and co-workers [120] report the case of an engineer from France who retired in Algiers and seven months later developed trachoma in one eye and early trachoma in the other. He had never had

¶ References 106 to 126.

any contact with natives or servants. His contact must have been from rubbing his eyes after contact with bills or shaking hands with people. The abortive forms of trachoma are also more frequent in newcomers to an area such as Algiers. The infection may be made more serious by contamination with the Koch-Weeks bacillus. Reinfection with trachoma virus once it has been inoculated may be a factor in producing these milder forms.

The controversy regarding the virus of trachoma continues, but the inclusion body probably represents the virus. Although inclusions are less common today than they were 20 years ago, Hassouna [110] feels that this is because trachoma is milder now than it was several years ago. He feels that the infant probably develops trachoma from younger children and not from the parents. The child is more susceptible than is the adult to the disease. The author feels that in many cases the onset is that of an acute conjunctivitis and that trachoma frequently follows Koch-Weeks infection. Trachoma still presents a diagnostic problem. Some authors point out that follicles behind the tarsal conjunctiva are important. Herbert's pits in the upper limbus and infiltration and vascularization of the upper half of the cornea are important clinical diagnostic findings. The inclusion bodies in scrapings from the epithelium aid in diagnosis. Scar formation is another finding. Degeneration of the follicles is believed to be of considerable importance for diagnosis.

Poleff [116] insists that the trachoma virus has been cultivated and feels that the virus should be called para-Rickettsia trachoma, since the virus is not a true virus and is related more closely to the rickettsias than to viruses. Nearly all the wide-spectrum antibiotics and sulfonamides appear to be effective in treatment against trachoma.

Mitsui and co-workers [127] were able to isolate a toxic substance from cases of trachoma that would produce a follicular conjunctivitis similar to trachoma in the acute stages, but with no evidence that the virus was present in the conjunctiva.

Epidemic Keratoconjunctivitis

This important disease has been the subject of considerable controversy in the literature during the past year. Cochburn [128] feels that it is advisable to review critically the present-day knowledge of epidemic keratoconjunctivitis. He critically reviews all the published reports of epidemics in the United States since 1936, beginning with the West Coast epidemic and extending through the United States to New York and New York State and then to the Middle West and to Windsor, Ontario. The largest epidemic probably occurred in Hawaii, where there were 10,000 cases, and nearly a 100% developed corneal opacities. The virus originally isolated by Sanders and Alexander has probably been lost, since it no longer neutralizes serum from patients who convalesced from the disease, as it did originally. Cockburn [128] states that at the time of writing no virus was available as a probable cause of epidemic keratoconjunctivitis. In a review of the epidemiology of the disease, he concludes that a latent infection may be activated by exposure to ultraviolet light. Trauma to the eye may precipitate a latent infection. The clinic may be the focus of the infection, and trauma to the eye may merely bring people to the clinic. Medical attendants and physicians are particularly liable to infections. The reservoir of the virus between epidemics is not known, but Cochburn [128] feels that there are at least five possibilities:

1. Serial passage from patient to patient
2. Cases of infection existing without keratitis but with mild conjunctivitis (these cases are capable of causing a classical epidemic disease under proper circumstances)
3. Presence normally of the agent in an inapparent form in the population, with activation of certain stimuli, in a way similar to that in which herpes simplex is stimulated
4. Symptomless carriers
5. An animal reservoir

He feels that further study is needed in order to decide as to the etiology, the epidemiology, and the methods of transmission of the disease.

Mitsui and co-workers [129] used clinically typical epidemic keratoconjunctivitis to indicate the influence of age of the patients on the clinical symptoms and severity of the disease. He says that the nursing infant less than 2 months of age seems to be incapable of forming follicles. Follicle formation, however, is the rule beginning at about 2 years of age, and increases rapidly at about 10 years of age, when a marked follicular reaction will occur. The preauricular node reaction shows a similar course except that the age at which this node appears is a little higher. The lymph node will be present from the ages of about 5 to 60 years. It is interesting that the amounts of reaction present in the infant and in the older age group are similar. The older the patient the slighter the reaction in the conjunctiva, and the younger the patient the less the reaction to the virus. The systemic disease that sometimes occurs with epidemic keratoconjunctivitis (fever, malaise, and generalized illness) is greater in the infant and in older persons than it is in the middle-aged group. The tendency toward membrane formation is marked in the older patients and in the very young infants.

Hofmann and Presinger [130] attempted to isolate the virus of epidemic keratoconjunctivitis. They were able to transfer an agent from one human volunteer to another and also to animals. If virus suspensions were dropped into the conjunctival sac of rabbits and guinea pigs, the results were negative. Likewise, no reaction occurred if human conjunctiva was implanted into the conjunctiva of rabbits and guinea pigs or if it was transferred into the anterior chamber of the eye. If the cornea was scarified prior to the inoculation, a mild keratitis was observed. They claim to be able to grow the virus in Maitland cultures and on developing hen's eggs which had previously been inoculated with corneal tissue, in a manner similar to the work of Sezar, reported in last year's review. Neutralizing antibodies were found in human serum. Filtration experiments show that the virus was between 50 and 80 mμ in diameter, and the virus particles could be demonstrated in electron-microscopic studies of tissue cultures and material from human conjunctiva. In the electron microscope these particles seem to be between 55 and 66 mμ. They were able to prove the infectivity of their cultures by inoculating animals and human volunteers.

There has been an epidemic in Switzerland. Verrey [131] presents the clinical history of 16 cases. In one family he saw a father and a son affected. All the other cases occurred individually. All the 16 patients recovered except for one, who had some corneal infiltrates. Babel, in discussing this paper, said that since March, 1954, they had had an epidemic in Genoa. Verrey [131] answered this by saying that Zurich was probably the first place in which the epidemic occurred when it came from Germany. The epidemic started in the summer of 1953, when they had 80 cases, and since then the number had decreased, so that in 1954 only 40 cases were seen. They were unable to isolate the virus at Zurich. There was no specific treatment. In Lausanne, Rosselet reported an epidemic in 1953 but few cases in 1954. He stated that good results were obtained with a mixture of oxytetracyeline (Terramycin) and cortisone. Goldman stated that in Bern they had an epidemic in the fall of 1953, which probably was propagated by the use of a tonometer. Of these 56 cases occurring in his clinic, the infection in 28 was passed by the tonometer. They were able to stop the epidemic in two days by sterilizing the tonometers. They threw out all the drops and fluids in the clinic, and the tonometers were sterilized. Since that time they have had only sporadic cases.

Cockburn and Danielson [132] followed an epidemic in Denver, where four persons were seen. The disease was originally passed from the original patient to the ophthalmologist and to the ophthalmologist's wife and one other person. The ophthalmologist developed severe corneal opacities. Two of the patients were treated with the serum from the original patients. The patient's serum was used as drops in the eyes of two patients. It may have been of some value in

treatment. Ormsby and Fowle [133] followed an epidemic in the Windsor, Ontario, industrial plant. They were unable to isolate the virus in mice; however, there was some indication that mice became ill after an inoculation. The authors used cortisone in an attempt to increase the incidence, but it apparently only brought out a mouse encephalitis virus, which was related to Theiler's virus.

While the material is not available for review at the time of writing, Ormsby and Fowle, Thygeson and Kimura, and others # have apparently been able to isolate a virus from cases similar to epidemic keratoconjunctivitis by various methods, which will be discussed below. Wiedersheim [134] states that epidemic keratoconjunctivitis frequently follows injury from corneal foreign bodies. He feels that the disease may be a compensation to injury. It may be that the infection is introduced by instruments. He says, however, that it is amazing that the infection starts in the conjunctiva, and not in the cornea, where the original injury occurred. In his clinic 15% of the cases had a history of previous injuries. The majority of cases, however, still occur spontaneously.

Trüb [135] reports on epidemic keratoconjunctivitis in Düsseldorf County, Germany. He states that there was a concentration of the disease in the cities in Northwest Germany because of the industry. The County of Düsseldorf has a population of 4,800,000. During the three-year period they had 10,366 cases. There were 4061 cases in 1952; 5887 in 1953, and only 418 in 1954. The highest incidence of the disease was either in the fall or in the spring. Most of the patients were in the middle-aged group, between 35 and 60; 60% were males and 38% were females. Most of the cases occurred in the heavy-industry area. The iron dust may cause small injuries, which may help to induce the disease. The frequency of ocular foreign bodies, however, increased the visits to the clinic for medical care and thus may contribute to the development of epidemic keratoconjunctivitis. Family transmission accounted for about 5% to 6% of all cases, while corneal opacities occurred in nearly all the patients. Only a few patients have permanent disturbance of vision.

Histology of Epidemic Keratoconjunctivitis.—Boeke [136] has studied the histology of a case of epidemic keratoconjunctivitis. This disease occurred in a 65-year-old man who had diabetic retinopathy and hemorrhagic glaucoma. Three weeks prior to his admission he developed epidemic keratoconjunctivitis and was admitted with the characteristic corneal infiltrate. He died one week after admission. The cornea showed subepithelial cellular infiltrates. These round-cell infiltrates occurred mostly in the superficial stroma and never reached deeper in the stroma. Most of the cells were lymphocytes; however, a few plasma cells and mononuclear cells were also present. Bowman's membrane was involved most prominently. It was thinned, folded, and interrupted. Where Bowman's membrane was absent, there was thickening of the epithelium to cover the defect. The author observed that the virus first breaks through the barrier of the epithelium, causing destruction of Bowman's membrane and an outpouring of the lymphocytes in the external stroma and epithelium. Later, the cells disappear and the defects are replaced by corneal epithelium or corneal stroma. While the corneal infiltrates were clearly visible in the living eye, histological examination showed only a few solid infiltrates, and Boeke [136] feels that some of these corneal changes must be produced by structural changes in Bowman's membrane, and not by cellular infiltrates. Compared with the corneal changes, the conjunctival changes are not characteristic. The conjunctival changes show that there is a predominance of lymphocytes and plasma cells. This picture may not represent the entire process, since the conjunctiva had already passed five weeks of inflammation. The cellular infiltrates were exclusively in the subepithelial layer, whereas the deeper conjunctival tissue was not affected. Most of the changes were found in the uper fornix. No follicles were present. The conjunctival epithelium showed

Personal communications to the author; papers to be published soon.

an uncharacteristic edema and some nuclear changes. They could not demonstrate with certainty nuclear changes with any of the stains, although many of the nuclear changes suggested that there may have been intranuclear inclusions.

The treatment of epidemic keratoconjunctivitis continues to be a problem. Many authors have specific treatment. Most of the treatment is ineffectual; however, Junker [137] reported excellent results with acetylcholine, used as local eye drops. Junker [137] has treated very few patients, but he wishes to point out to other physicians, who see more cases, that they should try this form of therapy.

Adenoidal-Pharyngeal-Conjunctival Virus Inflammation (Greeley Disease)

Greeley's disease was reported in last year's review (Cockburn). Bell and co-workers [138] followed an epidemic near Washington, D. C., and Leesburg, Va., where they found over 300 cases. The cases were characterized by an acute respiratory illness associated with conjunctivitis. The disease occurred in epidemic form in the summer day camps and in two residential neighborhoods. The authors were able to isolate a virus from 80 patients. They have called the virus APC Type 3. Apparently, there are several types of the virus. These authors isolated the virus on HeLa cells. While most of the patients had conjunctivitis, the one outstanding feature was a pharyngitis. It is interesting that the time of the onset of the illness and the ability to isolate the virus was close. The virus could be isolated on the 1st day of the disease in 62% of the patients; on the 2d to the 5th day in 69%; on the 6th to the 9th day in 45%, and after the 10th day in very few. They were able to isolate the virus in 80 out of 186 attempts, but they were not able to isolate the virus from the eye as readily as from the throat. During the first day of the disease only 33% eye isolations could be made, while on the second to the fifth day 60% of the eye isolations were positive, and during the fifth to the ninth day 50% were positive. On the first day 100% of the throat isolations were positive; on the second to the fifth day 80% were positive, and after the sixth day only 15% were positive. As was described last year, the disease is usually characterized by high fever, which often spikes to 104 F, and usually lasts from three to six days. Pharyngitis is commonly associated with mild to severe sore throat. The conjunctivitis is a nonpurulent follicular type, has monocular exudate, and lasts from one to three weeks. They state that the symptoms may occur alone or in combinations when only a conjunctivitis or only a pharyngitis is present. The disease occurs in epidemic and in sporadic form in all age groups, but it is predominantly a children's disease. They feel that infected human beings are the chief source of spread of the infection. Exposure to the disease usually produces an illness. Healthy carriers were not an important source of the infection. Older persons are more likely to be immune. Contaminated swimming pools were suspected but were not proved as a source of the infection. They suggested the name of pharyngeal-conjunctival fever.

Parrott and co-workers [139] followed a small epidemic at the infectious and parasitic disease service, the National Institutes of Health, Bethesda, Md. They were likewise able to isolate the so-called APC, Type 3 virus, and all persons who had the disease developed neutralizing antibodies. The complement fixation test as performed on tissue culture was also positive. From the recent reports at the Association for Research in Ophthalmology at the meeting held in Atlantic City in June, 1955, it appears that epidemic keratoconjunctivitis and pharyngeal-conjunctival fever may be related diseases. All the viruses concerned seem to be closely related and can be differentiated on the basis of neutralizing antibody titers and complement fixation tests. The reports of Ryan and co-workers,* Ormsby and Fowle, and Kimura and co-workers would seem to indicate that epidemic keratoconjunctivitis may be causd by APC virus, Type 9. It is

* Personal communication to the authors.

possible that by this time next year a more complete answer may be available for this complex and interesting group of virus diseases. Most of the other virus diseases have been discussed in other reviews.

Ocular Glandular Syndrome of Parinaud

Müller [140] states that since the original description of Parinaud's conjunctivitis contained no bacteriologic examination and Parinaud described three cases of his disease, it was impossible to say what caused this disease. Parinaud already has a supernuclear lesion attributed to him. Müller [140] would like to follow Gifford's suggestion and call the disease "conjunctival-glandular syndrome of Parinaud." Müller [140] states that tularemia causes about 4.3% of the cases. In tularemia antibodies are present on about the 10th to the 14th day and can be demonstrated in the serum. Tuberculosis can also produce the syndrome, and at times the differentiation between the two may be quite difficult. Boeck's sarcoid produces a similar picture; however, in most cases of Boeck's sarcoid involvement of the eyeball itself may be advanced. The Leptothrix has been verified by special sections and has been grown in culture; it accounts for many cases of the disease. Lymphogranuloma venereum causes a similar disease, which may be very much more violent than most cases of the conjunctival-glandular syndrome. In the case of lymphogranuloma, however, the Frei test is a helpful diagnostic sign. The author also discusses cat scratch fever, or benign infectious lymphoreticulosis. Here the specific skin test may be of some advantage. The virus of Newcastle's disease produces a picture similar to the conjunctival-glandular syndrome. Antibodies present in the serum may be of some help in diagnosis, and in many instances it is possible to isolate the virus. Epidemic keratoconjunctivitis may be confused at times except that there are no gray nodules or granulomas on the conjunctiva and the disease can be diagnosed as soon as the typical corneal lesion is developed. Müller [140] states that in order to make a diagnosis a biopsy is necessary. The smears and cultures must be taken. A serological examination must be made, and the smears and cultures of the conjunctiva should include inoculations of developing hen's eggs. The skin reactions to the various substances may aid in diagnosis. Individual cases of cat scratch fever [141] and tuberculosis of the conjunctiva [142] have been reported. Both these diseases have been discussed in past reviews.

Leprosy

An interesting symposium on ocular leprosy was held at the Royal Society of Medicine.† Leprosy is a systemic disease. The disease takes two main forms, the so-called lepromatous and the tuberculoid. The lepromatous form is characterized by widespread involvement of the skin, mucous membranes, nerves, bone marrow, some of the internal organs, and the eye. There is little or no attempt of the tissue to react or to localize the infection. In the tuberculoid form of the disease the infection is much more restricted. Often only certain areas of the skin and local lymph nodes or certain nerves are involved. Bacilli in the lesions are few, and the tissue reaction produces localization. In the lepromatous form the infiltration in the eye is very common and may produce no symptoms. The disease is common in India and in West Africa, where severe lepromatous infiltrations of the eye are seen. In Kashmir over 50% of the patients are partially or completely blind. Lowe [143] states that before the introduction of sulfone therapy the prognosis for lepromatous leprosy was often bad. Death was usually accompanied by partial or complete blindness. Sulfones given orally in small doses and combined with cortisone locally or by subconjunctival injection have certainly helped many of the patients. In the acute forms of the lepromatous type treatment is most effective. In the tuberculoid leprosy the eyes sometimes escape; however, the face is involved and the skin around the eye may directly or indirectly be involved. This includes the conjunctiva, the lids, and the cornea. Choyce [144] says that one of the

† References 143 to 145.

common features is anesthesia of the cornea and conjunctiva, which is due to the involvement of the fifth nerve. Since there is so much anesthesia, trichiasis causes no symptoms and the patients frequently refuse surgical correction for this reason. The trichiasis, therefore, causes considerable damage to the cornea. The seventh nerve becomes involved, and there may be severe atrophy of the superior part of the orbicularis muscle. The loss of winking and blinking produces an exposure keratitis. There is also secondary loss of eyelashes and eyebrows. This is called madarosis. Lepromata frequently occur on the upper lid but are very uncommon on the lower lid. Dacrocystitis, secondary to the collapse of the nasal cartilage, may occur. The corneal lesions account for a substantial part of the blindness. Leprosy is predominantly an anterior segment disease, in which the bacilli are numerous and the tissue reaction may be minimal. The treatment with the sulfones and cortisone has certainly helped a great deal in the management of the eye disease. It is interesting to note that Choyce [144] has seen no evidence of rapid multiplication of the bacilli under cortisone therapy. He wishes to stress the use of the sulfones but states that cortisone should be used early in the disease. Kirwan [145] says that lepra bacilli, or Mycobacterium leprae, are frequently found in conjunctival secretion and in biopsy specimens from the clinically healthy eyes. Congestion of the conjunctiva does occur. It may be limited or diffuse. Congestion of the conjunctiva may be limited to a triangular area on the side of the cornea. When nodules occur in the conjunctiva, as they sometimes do, the bacilli do not proliferate. They may be found in large numbers, however, in the episcleral tissue and under the surface of the sclera, close to the corneoscleral junction, where the anterior ciliary nerves penetrate. Kirwan [145] states that corticotropin and cortisone, in spite of their immediate striking effect, have produced considerable increase in symptoms. Some workers have obtained good results with small doses, while others have found that when the treatment is stopped, there is an acute exacerbation of the disease and an increase in the underlying infection. Cochrane,[145] in discussing these papers, states that cortisone should be used to prevent serious effects of ocular leprosy. He also says that it should be used very carefully while specific therapy is continued. Most authors are agreed that surgery on the eyes should be postponed unless there is considerable seriousness attached to the disease of the eyes. Once the eyes are operated upon, changes occur which cannot be controlled with therapy.

Toxoplasmosis

Abreu-Fialho [146] was able to produce a very interesting conjunctivitis in rabbits with Toxoplasma. He placed small pieces of cotton in the peritoneal fluid of mice which had been previously infected with Toxoplasma. These pieces of cotton were placed in the lower fornix of rabbit eyes and left there from one to four hours. Sixty rabbits were used in the experiments. The reaction in the conjunctiva varied. In some rabbits there was very severe conjunctivitis and in others it was mild. About one-third of the rabbits did not develop any conjunctivitis. The severity of the conjunctiva did not depend upon the dilution of the peritoneal fluid or upon the length of time the material was in contact with the conjunctiva. If a secondary infection occurred, then the Toxoplasma would usually reach the brain and produce a fatal encephalitis. The author feels that in some cases the conjunctiva of human beings may act as a portal of entry for Toxoplasma, and some cases have been described, according to this author. If the conjunctivitis is acute and severe, corneal ulceration usually develops. The interior of the eye was rarely affected. Lymph nodes were always involved in the adjacent cases.

Precancerous Melanosis of the Conjunctiva

Greer [147] disagrees with Reese [148] on many of his conclusions. He states that Reese [148] distinguishes sharply between precancerous melanosis and the pigmented junction nevi on the grounds that the nevus is a congenital circumscribed elevated lesion that rarely be-

comes malignant and is radioresistant. Precancerous melanosis, on the other hand, is acquired in adult life, is flat and diffuse, invariably becomes malignant, and is radiosensitive in its early stages. Greer [147] contends that these observations were made in a small series of cases. Reese [148] has collected cases from many areas and reports on 134 cases, which fall into the following groups: 37 cases of precancerous melanosis; 64 cases of cancerous melanosis; 28 cases of malignant melanomas of the conjunctiva, arising from the nevus, and 5 intermediate cases of what was questionable precancerous melanosis or malignant melanoma. Greer [147] contends that pigmented lesions of the conjunctiva lead to precancerous melanosis or malignant melanoma and states that precancerous melanosis does not always become malignant. Both Greer and Reese feel that precancerous melanosis is a proliferation of the basal cells of the conjunctival epithelium. Greer [147] believes that it is analogous to Bowen's intraepithelial carcinoma, or the extramammary Paget's disease. Reese [148] showed an interesting animated movie film that followed a conjunctival precancerous melanosis over a period of 23 years. The areas changed markedly and on these two occasions practically disappeared. Reese [148] adds that besides there being a conjunctival type of acquired melanosis there is a stromal type. It may change considerably over a period of time and may not become cancerous. The cancerous melanosis has a mortality of, at least, 40% and is probably considerably higher. Reese [148] still contends that exenteration of the orbit is the treatment of choice for cancerous melanosis when the diagnosis can be established. The case reports of malignant melanoma of the conjunctiva ‡ strongly indicate that the basal cells of the conjunctiva are responsible for the melanotic growth. The tumors may be pedunculated,[150] or they may be sessile.[149]

Primary epithelial malignant tumors of the palpebral conjunctiva are extremely rare. Halbertsma [151] reported a 68-year-old woman who complained of irritation in the conjunctiva. An irregular, completely thickened mass was found on the palpebral conjunctiva of the upper tarsal area in the right eye. The tumor was removed from the tarsus, with considerable bleeding. It proved to be a squamous-cell carcinoma. Five months later there was a recurrence, which was treated with x-rays. Since then there has been no recurrence. The tumor mass was clinically difficult to differentiate from trachoma and vernal conjunctivitis because of the elevated masses on the tarsal conjunctiva.

‡ References 149 and 150.

The Mucocutaneous Syndrome

The disease known as Bechet's disease, which is a recurrent genital and oral ulceration associated with eye lesions, is well presented by Phillips and Scott.[152] They present 10 cases that have been followed for the past three and a half years. The patients varied in age from 11 to 48 years. The genital, oral, and ocular lesions most frequently occur at different times. Pain in the genital region notably precedes the appearance of an ulcer by several days. The pain may be incapacitating in severity. Several patients with ulcerative lesions in the mouth could not eat their normal diet because of the painful oral lesions. In one of their patients 14 years elapsed between the initial onset of the oral lesions and the development of the eye lesions, the first genital lesion having appeared three years before. The genital lesions are characterized by excavation and fenestration of the labia minora. The whole vulva may be partially destroyed by successive outbreaks of the inflammatory process. Healing, when it takes place, is usually associated with considerable scarring. They were also able to find lesions in the vagina and on the cervix, which were associated with profuse discharge. They were unable to demonstrate any organisms in culture. The oral lesions were similar to the genital lesions but tended to be smaller. They occurred on the lips, the tongue, and the buccal surface of the cheek. The authors also found lesions on the hard and the soft palate. The eye lesions usually

begin with an inflammation of the conjunctiva, and each subsequent attack tends to be severer until iridocyclitis eventually develops. One of their cases resulted in complete blindness. Skin lesions are transient and inconsistent. When they are present, they resemble erythema nodosum. The authors state that the diagnosis of Bechet's disease is frequently missed because the patient receives only a specialized examination from an ophthalmologist, a dermatologist, a dental surgeon, or a gynecologist. Each of these specialists should be cognizant of the disease. The etiology is still obscure in their opinion. They feel that the disease is related to the collagen diseases. They completely discount the view taken by Sezar on the basis that other authors have been unable to isolate a virus. There are no antibiotic agents that are effective. Four of their ten patients were treated with cortisone, and all responded favorably. It is interesting that Derncourt [153] states that in younger girls there is usually a flare-up of symptoms of one of the lesions during the menstrual period.

The Johnson-Stevens syndrome (erythema multiforme exudativum) continues to be a disease with varied clinical manifestations. Corticotropin and cortisone § appear to be effective in treatment.

Ocular pemphigus is a destructive disease of the submucosa of the conjunctiva and a replacement by new connective tissue, according to Simpson.[156] The first stage of the disease is a catarrhal conjunctivitis with a ropy discharge. Episodes of secondary purulent infection occur. There are remissions with the disease, and at times the conjunctivitis will almost disappear. The vision is disturbed after exposure keratitis, and corneal ulceration occurs. Finally, ankyloblepharon and painful blindness occur, until death from generalized pemphigus or other cause ensues. The early recognition of pemphigus is difficult unless the skin or other mucous membranes are affected. Simpson [156] feels that there is no effective therapy.

University Hospitals.

§ References 154 and 155.

REFERENCES

1. Fazakas, A.: Congenital Anomalies and Mechanism of the First Part of the Afferent Apparatus, Ophthalmologica **129**:99-106 (Feb.) 1955.

2. Hopkins, W. G.: Treatment of Tearing in the Infant, Rocky Mountain M. J. **52**:132-134 (Feb.) 1955.

3. Cassady, J. V.: Management of Obstruction of the Lacrimal Duct, J. Internat. Coll. Surgeons **23**:836-840 (June) 1955.

4. Hurd, A. C.: Congenital Dacryostenosis, J. Maine M. A. **46**:12-14 (Jan.) 1955.

5. Jarlot, R.: Treatment of the Eye That Tears, Rev. prat. **4**:2197-2200 (Sept. 21) 1954.

6. Herrenschwand, F.: Epiphora in Older Patients, Klin. Monatsbl. Augenh. **125**:657-662, 1954.

7. Hubbard, W. B., and Hubbard, W. C.: Chronic Tearing (Lacrimation and Epiphora): Severing of the Lacrimal Ductules, J. Michigan M. Soc. **54**:574-576 (May) 1955.

8. Mattsson, R.: Mycotic Canaliculitis as a Cause of Persistent Lacrimation and Conjunctivitis, Nord. med. **53**:320-321, 1955.

9. Jeffery, M. P.: Lacrimal-Sac Obstruction, Am. J. Ophth. **38**:870 (Dec.) 1954.

10. Dunnington, J. H.: Congenital Alacrima in Familial Autonomic Dysfunction, A. M. A. Arch. Ophth. **52**:925-931 (Dec.) 1954.

11. Riley, C. M.; Freedman, A. M., and Langford, W. S.: Further Observations on Familial Dysautonomia, Pediatrics **14**:475-480 (Nov.) 1954.

12. Radnót, M., and Wallner, E.: Keratoconjunctivitis Sicca in Children, Ophthalmologica **128**:355-358 (Dec.) 1954.

13. Gurling, K. J.; Bruce-Pearson, R. S., and Pond, M. H.: Sjögren's Syndrome Treated with ACTH, Brit. J. Ophth. **38**:619-625 (Oct.) 1954.

14. MacLean, K., and Robinson, H. S.: Sjögren's Syndrome, Canad. M. A. J. **71**:597-599 (Dec.) 1954.

15. Parret, J.: Stomatologic Signs of Gougerot-Sjögren Syndrome, Ann. ocul. **187**:898-907 (Sept.) 1954.

16. Rubin, M. R.: Egg White in Treatment of Keratoconjunctivitis Sicca, Eye, Ear, Nose & Throat Month. **34**:50-51 (Jan.) 1955.

17. McEwen, W. K., and Kimura, S. J.: Filter-Paper Electrophoresis of Tears: I. Lysozyme and Its Correlation with Keratoconjunctivitis Sicca, Am. J. Ophth. **39**:200-202 (Feb., Pt. 2) 1955.

18. Radnót, M., and Németh, B.: Effect of Testosterone on the Lacrimal Gland, Ophthalmologica **129**:376-380 (June) 1955.

19. Nover, A.: Animal Experimentation on the Regeneration and Transplantation of Lacrimal Gland on Local and General Hormone Stimulation: II., von Graefes Arch. Ophth. **156**:98-118, 1954.

20. Nover, A.: Examination of the Function of the Lacrimal Gland in Rabbits, von Graefes Arch. Ophth. **156**:177-190, 1955.

21. Nover, A.: Experimental Examination of the Behavior of the Lacrimal Gland After Partial Extirpation, Zentralbl. allg. Path. **92**:339-346 (Oct.) 1954.

22. Forrest, A. W.: Epithelial Lacrimal Gland Tumors: Pathology as a Guide to Prognosis, Tr. Am. Acad. Ophth. **58**:841-847 (Nov.-Dec.) 1954.

23. Jones, I. S., and Pfeiffer, R. L.: Lacrimal Gland Tumors: Roentgenographic Diagnosis, Tr. Am. Acad. Ophth. **58**:841-1847 (Nov.-Dec.) 1954.

24. Arnold, I. L.: Unilateral Exophthalmos Due to Lacrimal Gland Cyst, J. Tennessee M. A. **48**: 11-12 (Jan.) 1955.

25. Romanes, G. J.: Dacryocystorhinostomy: Clinical Report of 50 Cases, Brit. J. Ophth. **39**:237-240 (April) 1955.

26. Hefel, F.: Experiences with the Dacryocystorhinostomy, Ophthalmologica **128**:61-69 (July) 1954.

27. Milder, B.: Lacrimal Fistula, a Surgical Technique Based on Dacryocystography, Am. J. Ophth. **39**:220-222 (Feb., Pt. I) 1955.

28. Iliff, C. E.: A Simplified Dacryocystorhinostomy, Tr. Am. Acad. Ophth. **58**:590-592 (July-Aug.) 1954.

29. Mahlen, S.: Talcum Powder Granuloma Following Dacryocystectomy, Nord. med. **52**:1311-1312 (Sept.) 1954.

30. Hallermann, W.: Pseudotuberculosis of the Tear Sac, Klin. Monatsbl. Augenh. **126**:59-62, 1955.

31. Jones, L. T.: Epiphora: Its Causes and New Surgical Procedure for Its Cure, Am. J. Ophth. **38**:824-831 (Dec.) 1954.

32. Fisher, B.; Zuckerman, G. H., and Douglass, R. C.: Combined Inheritance of Purpura Simplex and Ptosis in 4 Generations of One Family, Blood **9**:1199-1204 (Dec.) 1954.

33. Berke, R. N., and Wadsworth, J. A. C.: Histology of Levator Muscle in Congenital and Acquired Ptosis, A. M. A. Arch. Ophth. **53**:413-428 (March) 1955.

34. Johnson, C. C.: Blepharoptosis: A General Consideration of Surgical Methods, with the Results in 162 Operations, Am. J. Ophth. **38**:129-162 (Aug.) 1954.

35. McEvitt, W. G.: A Method for Correction of Blepharoptosis, J. Internat. Coll. Surgeons **23**:805-809 (June) 1955.

36. Lasky, M. A.: Ankyloblepharon Filiforme Adnatum, A. M. A. Arch. Ophth. **53**:882-883 (June) 1955.

37. Swan, K. C.: The Syndrome of Congenital Epiblepharon and Inferior Oblique Insufficiency, Am. J. Ophth. **39**:130-136 (April, Pt. 2) 1955.

38. Thevenard, A.: The Rapid Clinical Diagnosis of Myasthenia in Its Beginning, Presse méd. **63**:21-22 (Jan. 7) 1955.

39. Schilf, E.: Bilateral Total Ophthalmoplegia in Myasthenia Gravis Pseudoparalytica with Discussion of the Neuromuscular Connections, Nervenarzt **26**:214-216 (May) 1955.

40. Jacobs, H. B.: Strength of the Orbicularis Oculi, Brit. J. Ophth. **38**:560-566 (Sept.) 1954.

41. Fabing, H. D.: Alpha-(2-Piperidyl) Benzhydrol Hydrochloride, a New Central Stimulant, in the Treatment of Blepharospasm, Spasmodic Torticollis and Narcolepsy, Tr. Am. Neurol. A. **79**:159-163, 1954.

42. Higuti, Y.: An Experimental Study on the Development of Elastic Fibers, Okajimas folia anat. japon. **26**:187-190 (July) 1954.

43. Butler, J. B. V.: A Simple Operation for Correction of Senile Entropion, Eye Dig. **1**:3 (July) 1955.

44. Spina, V., and Pernet, A.: Repair of Ectropion of the Lower Lid, An. paulist. med. e cir. **68**:85-94 (Aug.) 1954.

45. Fox, S. A.: Lower Lid Repair, Tr. Am. Acad. Ophth. **58**:580-585 (July-Aug.) 1954.

46. Cole, J. G.: Repair of Severe Entropion of the Upper Lid, Am. J. Ophth. **38**:544-546 (Oct.) 1954.

47. Groenvall, H.: Plastic Restoration of the Upper Eyelid, Acta ophth. **32**:663-667, 1954.

48. Cutler, N. L., and Beard, C.: A Method for Partial and Total Upper Lid Reconstruction, Am. J. Ophth. **39**:1-7 (Jan.) 1955.

49. Beard, C.: Upper Lid Repair, Tr. Am. Acad. Ophth. **58**:586-589 (July-Aug.) 1954.

50. Gartner, S., and Chamlin, M.: Lid Mobilization and Tarsorrhaphy for Massive Proptosis, A. M. A. Arch. Ophth. **52**:234-239 (Aug.) 1954.

51. Callahan, A.: Loss of the Lower Fornix of the Anophthalmic Socket, Am. J. Ophth. **38**:75-78 (July) 1954.

52. Wies, F. A.: Surgery of Entropion, Am. J. Ophth. **38**:97 (July) 1954.

53. Callahan, A.: Senile Ectropion: Analysis of Types and Surgical Correction, Am. J. Ophth. **38**:787-790 (Dec.) 1954.

54. Bagóczky, L.: New Surgical Methods for Deformities Caused by Trachoma, Ophthalmologica **128**:54-57 (July) 1954.

55. Klemens, F.: A New Procedure to Shorten and Narrow the Palpebral Fissure, Klin. Monatsbl. Augenh. **126**:79-80, 1955.

56. Gifford, E. S., Jr.: Horizontal Excision of Tarsus in the Correction of Ectropion Luxurians, Am. J. Ophth. **38**:226-227 (Aug.) 1954.

57. Sayoc, B. T.: Plastic Construction of the Superior Palpebral Fold, Am. J. Ophth. **38**:556-559 (Oct.) 1954.

58. Feldstein, M.: Correction of Senile Atrophy of Eyelid and Blepharochalasis, Eye, Ear, Nose & Throat Month. **33**:605 (Oct.) 1954.

59. Roodyn, L.: Staphylococcal Infections in General Practice, Brit. M. J. **2**:1322-1325 (Oct.-Dec.) 1954.

60. Bahn, G. C.: The Treatment of Seborrheic Blepharitis, South. M. J. **47**:749-753 (Aug.) 1954.

61. Cohen, L. B.: Use of Selsun in Blepharitis Marginalis, Am. J. Ophth. **38**:560-562 (Oct.) 1954.

62. Theodore, F. H.: Differentiation and Treatment of Eczemas of the Eyelids, Tr. Am. Acad. Ophth. **58**:708-723 (Sept.-Oct.) 1954.

63. Theodore, F. H.: Ocular Eczema: Its Classification and Treatment, J. Mt. Sinai Hosp. **21**:255-269 (Jan.-Feb.) 1954.

64. Cope, S., and Jones, A. T.: Hemiplegia Complicating Ophthalmic Zoster, Lancet **2**:898-899 (Oct. 30) 1954.

65. Schenk, H.: Emphysema of the Lids, Klin. Monatsbl. Augenh. **125**:757-760, 1954.

66. Bose, J.: Phthiriasis Palpebrarum, Am. J. Ophth. **39**:211-215 (Feb.) 1955.

67. Kornblueth, W., and Liban, E.: Benign Calcified Epithelioma of Eyelid, Am. J. Ophth. **39**:208-210 (Feb.) 1955.

68. Christensen, L., and Fitzpatrick, T. B.: Keratoacanthoma of the Ocular Adnexa, A. M. A. Arch. Ophth. **53**:857-859 (June) 1955.

69. Brockhurst, R. J.: Mucocele of the Eyelid, A. M. A. Arch. Ophth. **53**:398 (March) 1955.

70. Gaul, L. E.: Syringoma of the Eyelids, A. M. A. Arch. Ophth. **53**:671-675 (May) 1955.

71. Sabri, J. A., and Diab, A.: Plexiform Neurofibroma of Orbit and Lid with Defects in Walls of Orbit and Involvement of Central Nervous System, A. M. A. Arch. Ophth. **52**:598-603 (Oct.) 1954.

72. Lockhart, C. E.: Surgical Treatment of Tumors of the Eyelids, Missouri Med. **51**:898-901 (Nov.) 1954.

73. Birkner, R., and Trautmann, J.: Contact Radiation as a Method of Choice in the Treatment of Lid Epitheliomas, Klin. Monatsbl. Augenh. **125**:445, 1954.

74. Robinson, R. C. V.: Comparative Incidence of Xanthelasma in Jews and Gentiles, A. M. A. Arch. Dermat. & Syph. **70**:662-663 (Nov.) 1954.

75. Robinson, R. C. V.: Treatment of Xanthelasma with Vitamin B_{12}, J. Invest. Dermat. **24**:111-113 (Feb.) 1955.

76. Friedman, M. W.: Congenital Symblepharon, Am. J. Ophth. **39**:236-237 (Feb.) 1955.

77. Goodside, V.: Ocular Findings in Hypercalcemia, Am. J. Ophth. **38**:856-858 (Dec.) 1954.

78. Schiff, F. S.: Cystine Deposits of Cornea and Conjunctiva, A. M. A. Arch. Ophth. **53**:434-436 (March) 1955.

79. Bloch, E. H.: The Bulbar Conjunctiva of Man as Site for Microscopic Study of the Circulation, Anat. Rec. **120**:349-361 (Sept.) 1954.

80. Passmore, J. W., and King, J. H., Jr.: Vital Staining of Conjunctiva and Cornea: Review of Literature and Critical Study of Certain Dyes, A. M. A. Arch. Ophth. **53**:568-574 (April) 1955.

81. Busacca, A.: Comments on Recently Appearing Articles on the Lymphatics in the Human Bulbar Conjunctiva, Arch. opht. **15**:5-9 (April) 1955.

82. Nataf, R.: Circulation of the Lymphatics in the Conjunctiva, Arch. opht. **15**:402-403 (Aug.) 1955.

83. Kronning, E.: Conjunctival and Corneal Stainability with Bengal Rose After Instillation of Local Anesthetics in Human Eyes, Am. J. Ophth. **38**:351-361 (Sept.) 1954.

84. Forster, H. W., Jr.: Rose Bengal Test, Am. J. Ophth.. **39**:253-254 (Feb.) 1955.

85. Kronning, E.: Rose Bengal Test, Am. J. Ophth. **39**:254 (Feb.) 1955.

86. Franke, J.: The Histamine Conjunctival Reaction as a Test of Focal Reactions, Klin. Monatsbl. Augenh. **126**:273-279, 1955.

87. Smith, C. H.: Bacteriology of the Healthy Conjunctiva, Brit. J. Ophth. **38**:719-726 (Dec.) 1954.

88. Soudakoff, P. S.: Bacteriologic Examination of the Conjunctiva: A Survey on 3,000 Patients, Am. J. Ophth. **38**:374-376 (Sept.) 1954.

89. Suie, T., and Taylor, F. W.: Incidence of Coagulase-Positive Staphylococci in External Ocular Infections, A. M. A. Arch. Ophth. **53**:706-707 (May) 1955.

90. Blender, W.: Ophthalmology in General Practice, Illinois M. J. **107**:114-120 (March) 1955.

91. Kimura, S. J., and Thygeson, P.: The Cytology of External Ocular Disease, Am. J. Ophth. **39**:137-145 (Feb., Pt. II) 1955.

92. Allen, J. H.: Principles of Treatment of Infectious Diseases of the Lids, Conjunctiva and Cornea, Mississippi Doctor **32**:78-81 (Aug.) 1954.

93. Ormsby, H. L.: Ophthalmia Neonatorum, Am. J. Ophth. **39**:90-95 (April, Pt. II) 1955.

94. Smith, C. A., and Halse, L.: Ophthalmia Neonatorum, Pub. Health Rep. **70**:462-470 (May) 1955.

95. Krahnstoever, M.: Chemical Keratoconjunctivitis, Klin. Monatsbl. Augenh. **126**:75-76, 1955.

96. de Saint-Martin, R.: Case Report of a Strange Foreign Body, Ann. ocul. **187**:825-827 (Sept.) 1954.

97. Ascher, K. W.: Study of 22 Malnourished Patients with Bitot's Spots, Am. J. Ophth. **38**:367-373 (Sept.) 1954.

98. Kamel, S.: The Pterygium: Its Etiology and Treatment, Am. J. Ophth. **38**:682-688 (Nov.) 1954.

99. Sie-Boen-Lian: Modification of the "Bare Sclera" Pterygium Operation, Ophthalmologica **128**:58-60 (Jan.) 1954.

100. Fritz, M. H.: Blindness from Multiple Pterygiums in an Alaskan Native, Am. J. Ophth. **39**:572 (April) 1955.

101. Purtscher, E.: Plant Therapy of Chronic Irritations of the Conjunctiva, Klin. Monatsbl. Augenh. **125**:715-719, 1954.

102. Theodore, F. H.: Newer Concepts of Vernal Conjunctivitis, Am. J. Ophth. **38**:859-860 (Dec.) 1954.

103. Alimuddin, M.: Vernal Conjunctivitis, Brit. J. Ophth. **39**:160-162 (March) 1955.

104. Foulds, W. S.; Greaves, D. P.; Herxheimer, H., and Kingdom, L. G.: Hydrocortisone in the Treatment of Allergic Conjunctivitis, Allergic Rhinitis, and Bronchial Asthma, Lancet **1**:234-235 (Jan. 29) 1955.

105. Bietti, G. B.: The Present Status of Virus Research in Ophthalmology, Wien. med. Wchnschr. **105**:412-418 (May 21) 1955.

106. Loisillier-Toulant, M.: The Diagnosis and Treatment of Trachoma, Rev. prat. **4**:2189-2196 (Sept. 21) 1954.

107. Button, R. R.: Treatment of Trachoma with Erythromycin: A Preliminary Report of 21 Cases, Am. J. Ophth. **39**:223-227 (Feb.) 1955.

108. Bietti, G.: Some Contributions to the Problems of Trachoma, Am. J. Ophth. **39**:112-130 (April, Pt. II) 1955.

109. Siniscal, A. A.: The Trachoma Story, Pub. Health Rep. **70**:497-507 (May) 1955.

110. Hassouna, M. A. L.: Trachoma in Brief, Am. J. Ophth. **38**:382-394 (Sept.) 1954.

111. Agarwal, L. P., and Saxena, R. P.: Erythromycin in Trachoma, Brit. J. Ophth. **38**:690-691 (Nov.) 1954.

112. Pavković-Bugarski, G., and Cvetojević, M.: Terramycin in Trachoma, Brit. J. Ophth. **38**:692-698 (Nov.) 1954.

113. Lazarus, A. S., and Farpour, M.: Relative Frequency and Mass Treatment of Trachoma in Southern Iran, Am. J. Ophth. **38**:665-673 (Nov.) 1954.

114. Agarwal, L. P., and Saxena, R. P.: Conjunctival Smear Cytology in Trachoma, Ophthalmologica **129**:93-98 (Feb.) 1955.

115. Siniscal, A. A.: The Trachoma Story, with a Discussion of Regional Problems, Rev. internat. trachome **31**:407-433, 1954.

116. Poleff, L.: The Actual State of the Principal Problems of Experimental Trachoma, Rev. internat. trachome **31**:434-483, 1954.

117. Rais, H.: Trichiasis Operations: Urgent Operations, Rev. internat. trachome **31**:484-486, 1954.

118. Pages, R.: Necessity That the Aim of Antitrachoma Campaign to Be More Preventive and Prophylactic Than Therapeutic, and Urgency Advice of the Medical Team, Rev. internat. trachome **31**:487-492, 1954.

119. Sie-Boen-Sian: Poleff's Epithelial Inclusion Bodies, Rev. internat. trachome **32**:177-184, 1955.

120. Pavković-Bugarski, G.: Role of Chlortetracycline (Aureomycin) and Oxytetracycline (Terramycin) in the Treatment of Trachoma, Ophthalmologica **128**:180-196 (Sept.) 1954.

121. Rev. internat. trachome **32**:155, 1955.

122. Mitsui Y.; Yamashita, K., and Hanabusa, J.: Treatment of Trachoma with Tetracycline, Rev. internat. trachome **32**:163, 1955.

123. Baron, J. B.: Studies on the Organic and Mineral Ions of the Sera of Trachomatous and of Patients with Vernal Conjunctivitis, Rev. internat. trachome **32**:168-176, 1955.

124. Baron, J. B.: Trachoma Control with Aureomycin in Nara, Japan, Rev. internat. trachome **32**:193, 1955.

125. Baron, J. B.: The Results of a Campaign Against Ocular Disease in Tunesia, Rev. internat. trachome **32**:185, 1955.

126. Toulant, P.; Larmande, A., and Loisillier-Toulant, M.: Abortive Trachoma of the Europeans: Its Frequency, Bull. Acad. Nat. Med. **138**: 260-263, 1954.

127. Mitsui, Y.; Tanaka, C.; Yamashita, K., and Hanabusa, J.: Toxin-like Substance of Trachoma Virus, A. M. A. Arch. Ophth. **52**:72-76 (July) 1954.

128. Cockburn, T. A.: The Present Status of Epidemic Keratoconjunctivitis, Am. J. Ophth. **38**: 476-485 (Oct.) 1954.

129. Mitsui, Y.; Tanaka, C., and Yamashita, K.: Change in the Constitution with Age, Its Influence on the Clinical Symptoms of Conjunctivitis, Am. J. Ophth. **39**:540-547 (April) 1955.

130. Hofmann, H., and Presinger, M.: Experimental Studies of the Virus of Epidemic Keratoconjunctivitis, Ztschr. Hyg. **141**:180-196, 1955.

131. Verrey, A.: Remarks on the Clinic and Therapeutics of Keratoconjunctivitis Superficialis So-Called Epidemic, Ophthalmologica **129**:261-270 (April-May) 1955.

132. Cockburn, T. A., and Danielson, R. W.: Epidemic Keratoconjunctivitis: Observations on 4 Cases, Am. J. Ophth. **38**:486-490 (Oct.) 1954.

133. Ormsby, H. L., and Fowle, A. M. C.: Epidemic Keratoconjunctivitis, Am. J. Ophth. **38**:490-495 (Oct.) 1954.

134. Wiedersheim, O.: Epidemic Keratoconjunctivitis and Accidents, Klin. Monatsbl. Augenh. **125**:107-109, 1954.

135. Trüb, C. L. P.: The Distribution of Epidemic Keratoconjunctivitis in Duesseldorf County in Northwest Germany from 1952 to 1954, Klin. Monatsbl. Augenh. **126**:180-202. 1955.

136. Boeke, W.: Histological Findings in Epidemic Keratoconjunctivitis, Klin. Monatsbl. Augenh. **125**:31-39, 1954.

137. Junker, H.: Treatment of Epidemic Keratoconjunctivitis with Acetylcholine, Klin. Monatsbl. Augenh. **126**:336-337, 1955.

138. Bell, J. A.; Rowe, W. P.; Engler, J. L.; Parrott, R. H., and Huebner, R. J.: Pharyngoconjunctival Fever, J A. M. A. **157**:1083-1092 (March 26) 1955.

139. Parrott, R. H.; Rowe, W. P.; Huebner, R. J.; Bernton, H. W., and McCullough, N. B.: Outbreak of Febrile Pharyngitis and Conjunctivitis Associated with Type 3 Adenoidal-Pharyngeal-Conjunctival Virus Infection, New England J. Med. **251**:1087-1090 (Dec. 30) 1954.

140. Müller, F.: The Differential Diagnosis of Ocular-Glandular Syndrome of Parinaud, Deutsche med. Wchnschr. **80**:152-154, 1955.

141. Wallace, F.: Cat Scratch Fever with Oculoglandular Syndrome, Memphis M. J. **29**:140 (Oct.) 1954.

142. Eadie, S.: Primary Tuberculosis of the Conjunctiva Treated with Streptomycin and P. A. S., Brit. J. Ophth. **38**:568-570 (Sept.) 1954.

143. Lowe, J.: Leprous Affection of the Eyes, Proc. Roy. Soc. Med. **48**:107-108 (Feb.) 1955.

144. Choyce, D. P.: Ocular Leprosy with Reference to Certain Cases Shown, Proc. Roy. Soc. Med. **48**:108-112 (Feb.) 1955.

145. Kirwan, E. W. O'G.: Ocular Leprosy, Proc. Roy. Soc. Med. **48**:112-118 (Feb.) 1955.

146. Abreu Fialho, S.: Experimental Toxoplasmosis Conjunctivitis in Rabbits, Wien. klin. Wchnschr. **66**:817-818 (Oct. 22) 1954.

147. Greer, C. H.: Precancerous Melanosis, Proc. Roy. Soc. Med. **47**:730-734 (Sept.) 1954.

148. Reese, A. B.: Precancerous and Cancerous Melanosis of the Conjunctiva, Am. J. Ophth. **39**:96-100 (April, Pt. II) 1955.

149. Agarwal, S. C., and Ahuja, M. L.: Malignant Melanoma of the Conjunctiva, with a Note on Its Histogenesis, Indian J. M. Res. **43**:365-366 (April) 1955.

150. Schaeffer, A. J.: Malignant Melanoma of the Upper Conjunctival Fornix, Am. J. Ophth. **38**:228-230 (Aug.) 1954.

151. Halbertsma, K. T. A.: An Epithelioma of the Tarsal Conjunctiva, Ophthalmologica **128**:1-6 (Jan.) 1955.

152. Phillips, D. L., and Scott, J. S.: Recurrent Genital and Oral Ulceration with Associated Eye Lesions, Bechet's Syndrome, Lancet **1**:366-370 (Feb. 19) 1955.

153. Derncourt, Y.: Bechet's Syndrome, Ann. ocul. **188**:556-571 (June) 1955.

154. Cutler, M.: ACTH in Stevens-Johnson Syndrome (Erythema Multiforme Exudativum), Am. Pract. & Digest Treat. **5**:612-613 (Aug.) 1954.

155. Hahn, H. J. A.: A Case of Stevens-Johnson Syndrome with Extensive Surgical Emphysema, Brit. M. J. **1**:1321 (May 28) 1955.

156. Simpson, D. G.: Ocular Pemphigus, Canad. M. A. J. **72**:921-923 (June 15) 1955.

ADDITIONAL REFERENCES

Curtin, B. J., and Theodore, F. H.: Ocular Molluscum Contagiosum, Am. J. Ophth. **39**:302-307 (March) 1955.

Lawrence, C. A.: Chemical Preservatives for Ophthalmic Solutions, Am. J. Ophth. **39**:385-394 (March) 1955.

Lebensohn, J. E.: Lid Paresis Induced by Oculo-Motor Akinesia, Am. J. Ophth. **38**:395-396 (Sept.) 1954.

Mascati, N. T.: Bowen's Disease, Am. J. Ophth. **38**:652-655 (Nov.) 1954.

Pau, H.: Sympathicolysis by Local Conjunctival Application of Opilon, Klin. Monatsbl. Augenh. **126**:171-176, 1955.

Webb, E. F.: Conjunctival Dermoid with Marked Seborrheic Component, A. M. A. Arch. Ophth. **52**:132-133 (July) 1954.

Witmer, R. H.: Antibody Formation in Rabbit Eye Studied with Fluorescein-Labeled Antibody, A. M. A. Arch. Ophth. **53**:811-816 (June) 1955.

Obituaries

JONAS S. FRIEDENWALD, M.D.
1897-1955

Jonas Friedenwald's death, on Nov. 5, 1955, is unquestionably one of the greatest possible losses to ophthalmology and to a host of scientific and non-scientific organizations. It is also a severe and irreparable shock to his many friends. Nor does the prior knowledge that he had inoperable carcinoma mitigate our distress at the final news that he has left us.

Jonas Friedenwald was a prominent member of a prominent Baltimore family. His father, Harry Friedenwald, had been for many years Head of the Department of Ophthalmology at the College of Physicians and Surgeons, Baltimore, and a distinguished figure in ophthalmic and Zionist circles.

Jonas was born in 1897 in Baltimore, educated in Baltimore (A. B., Johns Hopkins University, 1916; M.D., Johns Hopkins School of Medicine, 1920), and, except for occasional study periods elsewhere (M.A., Harvard, 1922), he lived continuously in Baltimore.

His catholic interest and authority made him a scholar in many fields. He was unquestionably one of this country's outstanding ophthalmic pathologists; he was also one of the foremost investigators, with specific interests in histochemistry, ophthalmic biochemistry, problems of intraocular fluid movement, and ophthalmic biochemistry in general. His publications, which number well over a hundred, reflect the diversity of his investigations and the universality of his interests. They are just a minor part, however, of the research he suggested, organized, and supervised.

He stimulated and trained innumerable young men and was always willing to interrupt his own pursuits for the purpose of helping others. He had the ability to analyze masses of data, discarding the irrelevant and extracting the solution with uncanny insight. In the laboratories of the Wilmer Institute when experimental findings resulted in confusion, Dr. Friedenwald could always be counted on to get to the basis of the difficulty and make pregnant suggestions for its resolution. His enormous fund of knowledge and experiences was eagerly sought by students, residents, clinicians, and research men in various fields at Hopkins and throughout the country. He could discuss on equal terms with the topflight specialists many complex phases of both basic science and clinical medicine. He gave freely of his advice and time and was extremely patient with the sincere student. He could be alarmingly stern, however, with those who wanted the "quick answer" or those whose intellectual honesty deviated the slightest. His quiet, subtle sense of humor and modest, unassuming manner were well known to all who came into contact with him. His clarity of thought and lucidity of expression enabled him to put even the most complicated problems across to his audiences—an accomplishment which made him a master moderator.

His ability to cope tactfully with administrative protocol and his high sense of ethics made him a favorite council, or on important committee posts. Withal he carried on a clinical practice and was known to be most sympathetic and painstaking in his handling of patients. In short, he was not only a great scientist, but a sensitive, understanding human being, whose selflessness, simplicity, and desire to help his fellow man made him loved by all.

Jonas Friedenwald was much honored in his lifetime. He received the Research Medal of the American Medical Association in 1935, the Howe Medal of the American Ophthalmological Society in 1951, and the first Proctor Award in 1948, and gave many of this country's formal lectures. Had it not been for his terminal illness he would have given the Doyne Lecture before the Oxford Ophthalmological Congress next July. At the time of his death he was Associate Professor of Ophthalmology at Johns Hopkins School of Medicine; a trustee of the Association for Research in Ophthalmology; a member of the Council on Neurologic Diseases

JONAS S. FRIEDENWALD, M.D.
1897-1955

and Blindness, Committee on Standardization of Tonometers, Radiation Cataract Committee, and many other local and national committees. He was an Associate Editor of the A. M. A. ARCHIVES OF OPHTHALMOLOGY, *Ophthalmologica*, and the *Journal of Histochemistry and Cytochemistry*. He was also an active member in the American Academy of Ophthalmology and Otolaryngology, American Medical Association, American Ophthalmological Society, American Society for Clinical Investigation, Ophthalmological Society of the United Kingdom, American College of Surgeons, and American Chemical Society.

Dr. Friedenwald enjoyed the isolation of vacations with his wife in the mountains. Here was the opportunity for long walks, the consumption of volumes of literature, and the development and elaboration of theories. In recent years he spent a month or two each summer in the Grand Tetons, of Wyoming, whence would come numerous long penciled letters expressing his latest ideas on current

research problems. The letters frequently contained pages of differential equations, quantitating the phenomena he was discussing. Long dissertations were often followed by "addenda" or "bulletins," with still newer concepts or corrections.

When he learned in August of his diagnosis and its poor prognosis, he wrote bravely and philosophically of his "firm determination to squeeze as much joy and interest, love and meaning out of the time still available as possible. Viewed in these terms the extent of that time is of less importance." In spite of untold difficulties and suffering during his remaining three months, he completed fundamental contributions on theoretical considerations of aqueous humor dynamics and on revisions of the calibration scales for tonometry and tonography. Such achievements as these will continue to inspire ophthalmologists in years to come.

It is with profound regret that we must record his passing. His friendship, wise counsel, and leadership will be sorely missed. His was a life that many may emulate, but few will achieve his stature. Our only solace is that his influence and ideals will live on in the minds and deeds of those many of us who have been fortunate enough to know him well.

DAVID G. COGAN
V. EVERETT KINSEY
BERNARD BECKER

Correspondence

CHORIORETINITIS PRODUCED BY ATOMIC BOMB EXPLOSION

To the Editor:—In my article, "Chorioretinitis Produced by Atomic Bomb Explosion," published in the ARCHIVES (**54**:539 [Oct.] 1955) I quoted from the Army hospital records of Fort Hood, Texas.

Unknown to me, this case was submitted for publication in *Military Medicine* (**117**: 338 [Oct.] 1955) by Dr. Arthur Lloyd Chambers, 2d, who was Chief of the Eye Section at the hospital in Fort Hood, Texas, and whose description of the lesion I have quoted in my article. The title of his article was "The Use of Cortisone in the Treatment of Chorioretinal Damage Resulting from Observation of Atomic Detonation."

Had this article been published in time to appear in the *Cumulative Index*, I would have given him credit for his observations and treatment of this case.

JACQUES LANDESBERG, M.D.
VA Regional Office
Brooklyn

News and Comment

GENERAL NEWS

American College of Surgeons.—The program of the meeting of the American College of Surgeons, to be held in Philadelphia, Feb. 15 and 16, 1956, is as follows:

8:00-12:00: Clinics in Local Hospitals

2:00-5:00 p. m.: South Garden, Bellevue-Stratford

SYMPOSIUM ON RECENT ADVANCES IN OPHTHALMOLOGIC SURGERY

Presiding: Harold G. Scheie, M.D., Philadelphia; Professor of Ophthalmology, University of Pennsylvania Graduate School of Medicine

Cataract Surgery
John M. McLean, M.D., New York; Professor of Surgery (Ophthalmology), Cornell University Medical College; Attending Surgeon-in-Charge (Ophthalmology), New York Hospital

Glaucoma Surgery
Paul A. Chandler, M.D., Boston; Associate Clinical Professor of Ophthalmology, Harvard Medical School; Surgeon, Massachusetts Eye and Ear Infirmary

Reconstruction of the Lids
Wendell L. Hughes, M.D., Hempstead, N. Y.; Clinical Professor of Ophthalmology, New York University College of Medicine; Advisory Attending Surgeon, New York Eye and Ear Infirmary; Attending Ophthalmologist, Nassau Hospital (Mineola, L. I.)

3:30-3:45: Intermission

3:45 p. m.: Present Status of Surgery of Retinal Detachment
Charles L. Schepens, M.D., Boston; Director of Retina Foundation and Clinical Associate, Harvard Medical School

4:15 p. m.: Lamellar Transplantation
R. Townley Paton, M.D., New York; Clinical Professor of Ophthalmology, New York University College of Medicine; Surgical Director, Manhattan Eye, Ear and Throat Hospital

OPHTHALMOLOGY

Thursday, February 16

8:00-12:00

Clinics in Local Hospitals

2:00-5:00 p. m. (South Garden)
Bellevue-Stratford

SYMPOSIUM ON MANAGEMENT OF EXOPHTHALMOS

Presiding: Albert D. Ruedemann, M.D., Detroit; Professor of Ophthalmology, Wayne University College of Medicine; Chief of Staff, Ophthalmology, Harper and City of Detroit Receiving Hospitals; Director and President, Kresge Eye Institute

Exophthalmos Due to Pathology in the Orbit or Adjacent Structures
Lorenz E. Zimmerman, M.D., Washington, D. C.

Endocrine Aspects of Exophthalmos
Edward Rose, M.D., Philadelphia; Professor of Clinical Medicine, University of Pennsylvania School of Medicine and Graduate School of Medicine; Chief, Endocrine Section, Medical Clinic, Hospital of the University of Pennsylvania

Treatment of Exophthalmos from the Viewpoint of the Internist
William Jefferies, M.D., Cleveland; Assistant Professor of Medicine, Western Reserve University School of Medicine; Physician-at-large, Endocrine Clinic, University Hospitals of Cleveland

Treatment of Exophthalmos from the Viewpoint of an Ophthalmologist
John W. Henderson, M.D., Rochester, Minn.; Associate Professor of Ophthalmology, the Mayo Foundation Graduate School of the University of Minnesota; Consultant, Section of Ophthalmology, Mayo Clinic; Ophthalmic Surgeon, Worrall Hospital

6:30 p. m.: Dinner and cocktails (sponsored by Section on Ophthalmology of the College of Physicians of Philadelphia), Warwick Hotel.
Tickets: $10. For reservations, write Dr. Harold G. Scheie, 313 S. 17th St., Philadelphia 3

Presiding: Dr. Harold G. Scheie, Chairman, Section on Ophthalmology, College of Physicians of Philadelphia

8:00 p. m.: Address by Paul A. Chandler, M.D., Boston; Associate Clinical Professor of Ophthalmology, Harvard Medical School; Surgeon, Massachusetts Eye and Ear Infirmary

French Optical Engineer, Back from Iran, Goes to Egypt on Second UNESCO Mission.—A French optical engineer who put an estimated $50,000 worth of optical instruments into working order during a 16-month stay in Iran is arriving in Egypt this month on his second mission for the United Nations Educational, Scientific and Cultural Organization.

The expert, P. M. Larraburu, will join in Egypt another French technician who worked for UNESCO in Iran, Pierre Biaunais, a laboratory glass blower. The two men, together with G. E. Fredericks, of the United States, a specialist in electrical and mechanical instruments, will be working in the laboratories of the Egyptian National Research Centre in Cairo, where maintenance workshops for scientific instruments are being opened.

Mr. Larraburu's mission is part of UNESCO's share in the United Nations world program of technical assistance for economic development. His mission to Iran sent him to the University of Teheran, where he repaired and adjusted

optical instruments used by the university, the Iranian Ministry of Agriculture, and a World Health Organization mission working in Iran. He also trained an assistant, who is now continuing his work.

Friedenwald Memorial Fund.—The death of Dr. Jonas S. Friedenwald, on Nov. 6, 1955, was an enormous loss to ophthalmic research and to the Association for Research in Ophthalmology.

In recognition of the profound interest in research and the brilliant accomplishments of Dr. Jonas S. Friedenwald, the trustees of the Association for Research in Ophthalmology announce the establishment of the Friedenwald Memorial Fund. The fund will be used for awards for meritorious research in ophthalmology and related sciences.

Contributions may be sent to any of the following committee members: David G. Cogan, M.D., Chairman, 243 Charles St., Boston; Bernard Becker, M.D., 640 S. Kingshighway Blvd., St. Louis 10; Dr. V. Everett Kinsey, Kresge Eye Institute, 690 Mullett St., Detroit.

SOCIETY NEWS

Ophthalmological Society of Egypt.—The annual meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, on Friday and Saturday, March 16 and 17, 1956, at 9 a. m. The symposium of this meeting will be on corneal grafting. Medical practitioners, oculists or otherwise, are cordially invited.

Royal Society of Medicine, Section of Ophthalmology.—The Royal Society of Medicine has assigned the following dates for meetings of the Section of Ophthalmology at the Society's house, 1 Wimpole St., London, W.1.

Meetings are held at 5 p. m. (cases at 4:30 p. m.)

Friday, Feb. 17, 1956 (joint meeting with Section of Radiology)
Thursday, March 8, 1956
Thursday, May 10, 1956
Thursday, June 14, 1956 (Annual Meeting)

The honorary secretaries of the section are J. E. M. Ayoub, F.R.C.S., 11 Wimpole St., London, W.1, and E. S. Perkins, F.R.C.S., 23 Goodyers Ave., Radlett, Herts.

ANNOUNCEMENTS

A. M. A. Annual Meeting, Chicago, June 11-15, 1956.—The 105th Annual Meeting of the American Medical Association will be held in Chicago, June 11-15, 1956, with a full program of lectures, television, motion pictures, and scientific exhibits.

The lecture program for each Section is prepared by the Section Secretary, and prospective participants should communicate as soon as possible with the Secretary of the Section before which they hope to read a paper. Application blanks for space in the Scientific Exhibit are now available and may be obtained from the Section Representative to the Scientific Exhibit.

Section on Ophthalmology

Secretary: Harold G. Scheie, M.D., 313 S. 17th St., Philadelphia 3.

Exhibit Representative: Frank W. Newell, M.D., 950 E. 59th St., Chicago 37.

Additional information may be obtained from the Secretary, Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10.

voted

"MOST HELPFUL"

to the doctor in bringing clean, clear vision.

Some of the reasons—true focus polish, corrected curves and blur free barium segments.

to the laboratory for being easy to process.

The reasons here—F's accurate curves, excellent polish, dependable results.

Continental INDIANAPOLIS

PRO or CON Beta Radiation of the Eye?

THE M-I STRONTIUM-90 APPLICATOR DESERVES YOUR INTEREST

Whether you, yourself, are doubtful or convinced of the merits of beta radiation therapy —or undecided—you'll be interested, we think, in the scientific data gathered together for you in our booklet, "Radiation Therapy Sources." In addition to its summary of clinical data, indications for treatment by irradiation, suggested dosage table, and description of our improved M-1 applicator, the booklet includes a brief summarization of U. S. Atomic Energy Commission regulations governing the purchase and use of this type of equipment. It's interesting, it's factual—and it's yours without obligation.

Write For Booklet, "Radiation Therapy Sources" — Yours On Request With Our Compliments

V. Mueller & Co.

330 SOUTH HONORE STREET
CHICAGO 12, ILLINOIS

BRANCHES NOW IN ROCHESTER (MINN.) — DALLAS AND HOUSTON, TEXAS

Complete ARTIFICIAL EYE *Service*

Experience gained through over 100 years of artificial eyemaking enables us to produce and fit the very finest in artificial eyes. Glass and plastic eyes made to order or available from stock. Eyes fitted to all types of motility implants

artificial eye selection through the mail

- Orders filled the same day received
- Eyes sent on memorandum
- Liberal assortment of either glass or plastic
- Samples accurately matched
- Superior quality eyes—Finest workmanship

WRITE FOR FREE COLOR CHART AND SIZE GUIDE

Serving the Profession Since 1851

Mager and Gougelman inc.

30 North Michigan Avenue, Chicago 2, Illinois : 510 Madison Avenue, New York 22, New York

DETROIT • CLEVELAND • KANSAS CITY • MINNEAPOLIS • ST. LOUIS
BOSTON • PHILADELPHIA • PITTSBURGH • WASHINGTON

More for your ℞ Dollar . . . from BENSON

More . . .

. . . when you know that *every* ℞ — no matter how simple or complex — is thoroughly analyzed, every lens is checked, tested, and inspected over and over again before it leaves a BENSON laboratory . . . *at no additional cost.*

More . . .

. . . when you consider the quality of material BENSON puts into each prescription — whether it be a tough +20.00 sph. on a −15.00 cyl. in a bifocal, or simply a low compound. BENSON OPTICAL *has never used a second quality lens.*

And More . . .

. . . when you realize that 42 years of continuous BENSON research and study have brought the very latest improvements in modern ℞ methods into BENSON laboratories — designed, equipped, and staffed to meet the everyday, as well as special, needs of the most discriminating doctors dedicated to good eye care.

That's why the name "Benson" has come to stand for quality and precision in ophthalmic optical production.

We invite your inquiries.

Since 1913 Benson OPTICAL COMPANY **Executive Offices • Minneapolis 2, Minn.**

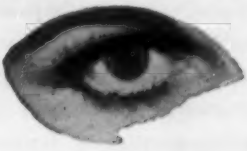
COMPLETE LABORATORIES CONVENIENTLY LOCATED IN UPPER MIDWEST CITIES

OPHTHALMIC INSTRUMENTS
OF PRECISION

Theodore Hamblin Ltd

GUILD Rx OPTICIANS

15 WIGMORE STREET,
LONDON, W.1.
ENGLAND.



Most Natural
ARTIFICIAL EYES

Dispensers and makers of fine eyes of plastic and glass. Eyes to fit all types of implants.

Selections sent on memorandum from the most complete group of eyes. Careful attention given to all referred cases.

The Doctor and his patient must be completely satisfied or there is absolutely no obligation.

Of Service Since 1906

DENVER OPTIC COMPANY

310 University Bldg. **Telephone Main 3-5638** **Denver 2, Colorado**

a frame for every face...

a trim for every frame...

RUMOR

for every woman

K-1 DELTA — pink, black and white tips

K-2 LARKSPUR

K-3 SHARON — pink, white and blue flowers

K-4 ALUKON — trim; brook blue, mellow copper, old rose, ebony, or oxford gray

K-5 KARAT TOP — 1/10 12 K yellow or white gold filled

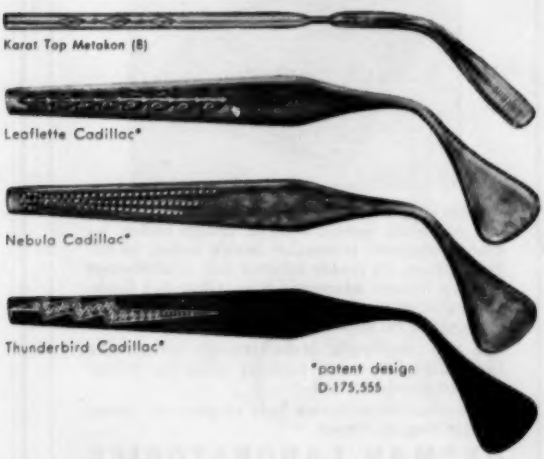
K-6 LEAFLETTE — 1/10 12 K yellow or white gold filled, also K-6A Leaflette trim in aluminized assorted colors

K-7 NEBULA — 1/10 12 K yellow or white gold filled

K-35
THUNDERBIRD
Trade Mark

Des. Patent Pending on Frame

KARAT TOP METAKON



Karat Top Metakon (B)

Leaflette Cadillac*

Nebula Cadillac*

Thunderbird Cadillac*

*patent design D-175,555

KONO MANUFACTURING CO. INC
Woodside, N. Y.
KONO SALES CO. INC.
Woodside, N. Y.

KONO OF THE SOUTH, INC.
Charleston, S. C. Atlanta, Ga.
KONO OF OHIO, INC.
Columbus, Ohio

© KMC

KONO Kono

KONO OF CALIFORNIA, INC.
Los Angeles, Calif.
KONO OF ILLINOIS, INC.
Chicago, Ill.

Rx

QUALITY SERVICE

Technical skills and services that will never let you down

DOW

Top-Grade Technical Performance

. . . a Safeguard for Your Professional Skills and Judgment.

¶Your prescriptions, conceived from your rich fund of scientific knowledge laboriously developed through years of study, training and experience, are at the mercy of the dispensers who interpret them. They will be safe in the hands of Dow seasoned craftsmen, whose devotion to the exacting standards which your professional reputation demands, and which our firm has consistently maintained throughout its 31 years of existence, is a guarantee of complete patient satisfaction.

DOW OPTICAL CO.

W. E. DOW, Pres.

Chicago, Ill. Bloomington, Ill.

The Berman Metal Locator

An electromagnetic detecting device that quickly and accurately locates metallic foreign bodies, including magnetic intraocular foreign bodies. Metallic fragments are readily detected from a satisfactory distance through intervening bone, tissue and fluids. Probing or physical contact with the foreign body is not required for detection.

The thin sterilizable probe provides preoperative localization, "pin-point" accuracy within the incision and postoperative check.

Lends precision to foreign body surgery and greatly reduces surgical trauma.

BERMAN LABORATORIES

112-03 Rockaway Blvd. Ozone Park 20, N. Y.

GILL MEMORIAL EYE, EAR AND THROAT HOSPITAL

Announces to the Profession

TWENTY-NINTH ANNUAL SPRING CONGRESS

in

OPHTHALMOLOGY AND OTOLARYNGOLOGY

April 2nd to April 7th, 1956

GUEST SPEAKERS

Rudolf Aebli, M.D., F.A.C.S.	New York, N. Y.
Samuel Blank, M.D.	Philadelphia, Pa.
John E. Bordley, M.D.	Baltimore, Md.
E. B. Burchell, M.D.	New York, N. Y.
Virgil S. Casten, M.D., F.A.C.S.	Boston, Mass.
Watson Gailey, M.D.	Bloomington, Ill.
Jack S. Guyton, M.D.	Detroit, Mich.
Bayard T. Horton, M.D.	Rochester, Minn.
Curwood J. Hunter, M.D.	Cincinnati, Ohio
John R. Lindsay, M.D.	Chicago, Ill.
John E. Magielski, M.D.	Ann Arbor, Mich.
Ross T. McIntire, M.D., F.A.C.S., F.I.C.S.	Chicago, Ill.
Dr. Stephen J. H. Miller, M.D., F.R.C.S.	London, Eng.
Peter N. Pastore, M.D.	Richmond, Va.
F. Johnson Putney, M.D.	Philadelphia, Pa.
Herbert J. Rinkel, M.D.	Kansas City, Mo.
Samuel Rosen, M.D.	New York, N. Y.
Russell A. Sage, M.D.	Indianapolis, Ind.
C. Dwight Townes, M.D., F.A.C.S.	Louisville, Ky.
Everett R. Veirs, M.D.	Temple, Texas
Henry P. Wagener, M.D.	Rochester, Minn.

For Further Information Write:

Superintendent, P. O. Box 1789 Roanoke, Virginia

GUILD Rx OPTICIANS

WHAT TYPE OF BIFOCAL?

When multifocal lenses are prescribed
the important question becomes what
type of lens to use. There are dozens
of types of lenses to choose from in
several hundred combinations.
Your GUILD OPTICIAN knows that each type
has its purpose and can fit your patient
with the lenses best suited for his needs.
Just another example of the teamwork
between ophthalmologist and optician
that results in better vision.

A NEW SERIES IN

SEX EDUCATION

Titles in the new series

- **PARENTS' PRIVILEGE**
  for parents of young children of pre-school and early school age
- **A STORY ABOUT YOU**
  for children in grades 4, 5, and 6
- **FINDING YOURSELF**
  for boys and girls of approximately junior high school age
- **LEARNING ABOUT LOVE**
  for young people of both sexes (about 16 to 20 years of age)
- **FACTS AREN'T ENOUGH**
  for adults who have any responsibility for children or youth that may create a need for an understanding of sex education

PRICES

Note: Discounts apply to quantities of any single title, or to quantities of sets.

Quantity	Discount	Price
1	—	$ .50
10	10%	4.50
25	30%	8.75
50	40%	15.00
100	50%	25.00
1000	60%	200.00

Set of 5 titles, $2.25.

Distributed By
Order Department

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St.
Chicago 10, Ill.

ORDER BLANK

Enclosed is $_____(no stamps) for the following pamphlet(s):

Title	Quantity
1. PARENTS' PRIVILEGE	
2. A STORY ABOUT YOU	
3. FINDING YOURSELF	
4. LEARNING ABOUT LOVE	
5. FACTS AREN'T ENOUGH	
Complete set of five	

Please send pamphlet(s) to:
(Please Print)

Name_____
Street_____
City_____
Zone_____ State_____

OP 1-56

Do you dispense glasses?

We are one of the oldest, and most reputable wholesale opticians in the east, serving the discriminate ophthalmologist.

An inquiry from you will bring a representative at your convenience to outline our superior service plan.

MAX ZADEK, INC.

established 1904

115 Fulton Street New York 38, N. Y.

I Hide Your Eyes

Says Gary Ghost

When a person has his picture taken wearing glasses, ever notice the reflections on the lenses? These are "ghost images." MAY-O-LITE, a Low Reflection Lens Coating, reduces reflections up to as much as 95 per cent, yet increases light transmission.

Complete Your Professional Service By Adding

The Best in Sight

MAY-O-LITE

Low Reflection Coating

MAY RESEARCH, INC., Box 1181, Minneapolis 1, Minn.

POSTGRADUATE CONFERENCE IN OPHTHALMOLOGY UNIVERSITY OF MICHIGAN MEDICAL SCHOOL

The Department of Postgraduate Medicine of the University of Michigan Medical School announces the annual conference in Ophthalmology for qualified physicians, April 23, 24 and 25, 1956, to be given at the Horace H. Rackham Graduate School Building, Ann Arbor, Michigan, under the direction of the Department of Ophthalmology.

GUEST LECTURERS

Dr. V. Everett Kinsey, Detroit, Michigan; Dr. Albert N. Lemcine, Jr., Kansas City, Missouri; Dr. Irving Henry Leopold, Philadelphia, Pennsylvania; Dr. P. Robb McDonald, Philadelphia, Pennsylvania; Dr. John S. McGavic, Bryn Mawr, Pennsylvania; Dr. Hugh L. Ormsby, Toronto, Canada.

MEMBERS OF STAFF

Dr. F. Bruce Fralick, Dr. Harold F. Falls, and Dr. John W. Henderson.

Complete program and details will be mailed upon request.

John M. Sheldon, M.D., Director

Department of Postgraduate Medicine

University Hospital Ann Arbor, Michigan

E. B. Meyrowitz

SURGICAL INSTRUMENTS CO., INC.
520 FIFTH AVENUE, NEW YORK 36, N. Y.
LONDON *ESTABLISHED 1875* PARIS

McLEAN TONOMETER

This is a most accurate instrument for measuring intraocular pressure. It is simple in construction and operation, has a direct reading scale with constant weight factor and does not require charts and nomographs. The scale shows normal and abnormal limits of tension in red and black.

Supplied in case, $55.00

LEBENSOHN NEAR VISION TEST CHART
(Revised 1947)

The use of both sides of this substantial chart permits the presentation of a wide variety of tests that will be found useful in office or clinic. Basically a miniature Snellen chart, it gives precise reading acuity expressed as distance equivalent, decimal or visual efficiency.

The newest edition has an accommodation or near test that is positive but simple to use; a duochrome test for near and a bead chain for fixing the working distance at 33 cm. The chart has reading types in English and Spanish, with type sizes and Jaeger equivalents as well as a near test for illiterates. Two sides as illustrated, in plastic covered frame with hanger and measuring chain.

Cat. No. B4285 **Price $7.50**

"Doctor, can you tell me . . . ."

What is it? What causes it? How serious is it?

For explanations to these questions and many more, have your patients read:

DIPHTHERIA
by Paul S. Rhoads, 8 pages, 15 cents

SCARLET FEVER
by E. B. Perry, 8 pages, 15 cents

WHOOPING COUGH
by Constance Frick, 4 pages, 10 cents

MEASLES
by A. L. Hoyne, 8 pages, 15 cents

PNEUMONIA
by W. W. Bolton, 12 pages, 15 cents

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

PRESCRIBE THIS

GUARANTEED PROTECTION

FROM LENS BREAKAGE

I-GARD prescription lenses are highly resistant to impact. Your I-Gard distributor is authorized to replace *free of charge* any I-Gard lens that does not successfully withstand accidental breakage from a hard blow—even one that would fragmentize any other lens—*glass or plastic.*

It is important to keep in mind that I-Gard lenses offer priceless eye protection with feather-light comfort. *How many of your wearers know this?*

Send for I-Gard Foci Charts . . . Price List . . . Samples . . . and name of nearest I-Gard Distributor.

really Feather-Light

really Non-Shatterable

i-gard

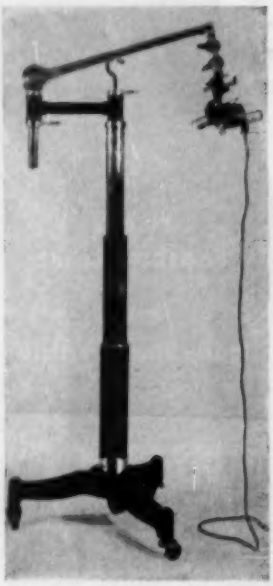
Worn by millions all over the world

DEPT. E

McLEOD OPTICAL COMPANY, INC.

357 Westminster Street, Providence 1, R. I.

i-gard Plastic Lenses



Gonioscope

Instrumentation for

MICRO-GONIOSCOPY and GONIOTOMY

after Otto Barkan, M.D.

GONIOSCOPE (illustrated) floor model, for office and hospital surgery	$185.00
CORNEAL MICROSCOPE B & L	180.00
CORNEAL MICROSCOPE Haag-Streit	225.00
Your own Corneal Microscope adapted to gonioscope	10.00
Otto Barkan Focal Illuminator (hand lamp) with plug in transformer	42.50
Otto Barkan-Koeppe Diagnostic Lens (for viewing the angle) small (infant) 16 & 17 mm (medium) 18 & 19 large (adult) 20 mm in glass	45.00
Otto Barkan Surgical Goniotomy Lens small (infant) med. (child and adult)	45.00
Otto Barkan Surgical Knife (latest model)	9.75
Otto Barkan Operating Lamp	65.00
Floor stand for above	20.00

PARSONS OPTICAL LABORATORIES, INC.

518–20 Powell Street San Francisco 2, Calif.

NEW YORK UNIVERSITY
POST-GRADUATE MEDICAL SCHOOL

offers you

- Graduate Courses in all specialties of Medicine and Surgery
- More than 100 Post-Graduate Courses
- Numerous special short Refresher Courses
- Clinical and Laboratory Facilities of N.Y.U.-Bellevue Medical Center and 20 affiliated hospitals

courses open to you include

- Neuro-Ophthalmology
- Differential Diagnosis with the Slit Lamp
- Anesthesiology
- And Many Other Courses in the Basic Sciences and General Medicine

For further information, write to:

NEW YORK UNIVERSITY - BELLEVUE MEDICAL CENTER
Post-Graduate Medical School
522 First Avenue • New York 16, N. Y.

DVORINE ANIMATED FUSION CHARTS

Set includes 68 charts in full color for Base-In and Base-Out home training directed by the doctor—especially for children—may also be used for adults. Prescribed by ophthalmologists for over 20 years.

Exclusive Features:

- Animation
- Nine Groups of Charts
- Gay Colors
- Vertical Fusion Device
- Tracing Sheets
- Duo-Chrome Spectacles and Drawing Outfit

ALL IN ONE SET:
(with directions)

Price $12.00

Less 5%, if check accompanies order.

Order direct from us or from your Optical Supply House.

SCIENTIFIC PUBLISHING CO.
Dept. A. 2328 Eutaw Place, Baltimore 17, Md.

As good
to look **at**
as it is good to
look **through**

Major Lens: Special Nokrome Crown glass. (Plus-power in the lenticular edge, though much weaker, allows patient some recognition of form in peripheral vision.)

Lenticular Field: Special high index barium glass.

Bifocal Segment: Same high index glass as lenticular field.

Fused Lenticular Panoptik Cataract Bifocal

Here's the lens to provide the greatest possible satisfaction to aphakic patients. It's lighter in weight, thinner—usually more than one third thinner than a one-piece bifocal of the same power—and has flatter front curves.

The Panoptik segment shape is ideally suited to the cataract patient. It offers a wide reading field at normal reading level. Flexibility, too, in base curves—bi-convex, plano base or −3.00 base—can be produced from the same blank. This facilitates service from the laboratory—a single pair of blanks, in each of the called-for reading additions, constitutes a stock from which any aphakic prescription can be made.

From both standpoints—cosmetic appearance and optical performance—the Panoptik Lenticular Cataract bifocal sets the standard of excellence.

In Soft-Lite, too

BAUSCH & LOMB

SINCE 1853

BVI

CHICAGO OPHTHALMOLOGICAL SOCIETY

1956 CLINICAL CONFERENCE

February 10-11, 1956 — ***The Drake Hotel***

Friday A. M.	
Symposium on Neuro-ophthalmology	Douglas Buchanan, M.D., Chicago Ben Lichtenstein, M.D., Chicago Wilbur Rucker, M.D., Rochester, Minn. Loyal Davis, M.D., Chicago
Friday P. M.	
Problems in Diagnosis and Treatment of Strabismus	Hermann Burian, M.D., Iowa City, Iowa
A New Autonomic Drug	David Rosen, M.D., New York, N. Y.
The Twelfth Annual Gifford Memorial Lecture	
Alterations in the Caliber of Retinal Vessels	Wilbur Rucker, M.D., Rochester, Minn.
Saturday A. M.	
Symposium on Diabetic Retinopathy	Rachmiel Levine, M.D., Chicago Henry Ricketts, M.D., Chicago David Rosen, M.D., New York Lester Coggeshall, M.D., Chicago
Saturday P. M.	
A New Scleral Shortening Operation	Ramon Castroviejo, M.D., New York, N. Y.
Clinical Application of Electroretinography	Hermann Burian, M.D., Iowa City, Iowa
Unusual Procedures in Cataract Extraction	Ramon Castroviejo, M.D., New York, N. Y.

take the hating out of waiting

MAKE YOUR READING RACKS COMPLETE

WITH A VARIETY OF PAMPHLETS

TO INTEREST YOUR PATIENTS . . .

An extensive selection of subjects, ranging from allergies to weight control. . . . Low single copy prices with liberal discounts on quantity orders:

10 copies	10%
25 copies	30%
50 copies	40%
100 copies	50%
1,000 copies	60%

CATALOG FREE UPON REQUEST

WRITE TO:

BUREAU OF HEALTH EDUCATION
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET • CHICAGO 10, ILLINOIS

gullstrand magnifying spectacles

magnified stereoscopic vision
combined with long working distance
for detailed observations,
examinations and operations.

Lightweight and comfortable, the Gullstrand Magnifying Spectacles provide a magnified image free of distortion and aberration over the entire field of view. With a long working distance and a wide field of view, the spectacles are extremely well adapted for detailed observation of every description. While working, the wearer can look past the magnifiers to obtain an unobstructed view of his surroundings.

Spectacle magnifiers with frames holding regular prescription glasses.

Precision made in the finest Zeiss tradition, the spectacles have full interpupillary adjustment and may be worn in conjunction with spectacle lenses. Price **$67.50** in beautiful new, lined leather case. Spectacle frames **$5** per pair.

Consult your dealer or write today for an interesting booklet describing the Zeiss Gullstrand Magnifying Spectacles in detail.

Scientific Instrument Division

ERCONA CORPORATION 551 FIFTH AVE., NEW YORK 17, N. Y.

(Actual size 13½" x 14")

SIMPLIFIED ASTIGMOMETER

(Lebensohn)

PLASTIC

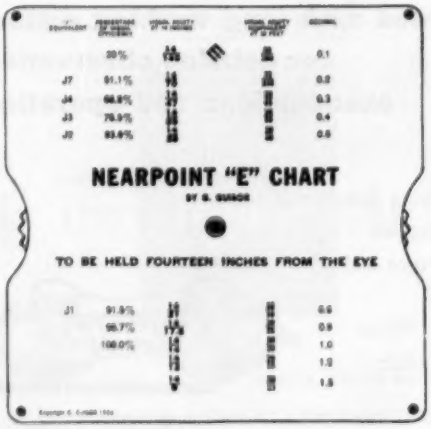
WASHABLE

"NO COMPUTATION REQUIRED"

CAN BE USED AT 10 OR 20 FEET

Send for Literature

EACH $9.75



Actual size 6" x 6"

New Near Chart

GUIBOR Symbol Near Chart now available in durable and soilproof plastic. Gives distance equivalents, as well as quantitative measurements for near vision. E Symbol understood by all.

Place your order now.

$3.25

DISPENSING SERVICE

Loop Office:
111 N. Wabash, at Washington
9th Floor STate 2-5362
CHICAGO, ILL.

Austin Belgard INC.
(Formerly Belgard, Inc.)

OPHTHALMIC OPTICIANS
WHOLESALE & SERVICE

Wilmette Office:
1139 Central Avenue
WILMETTE, ILL.

Beauty in Eyewear!

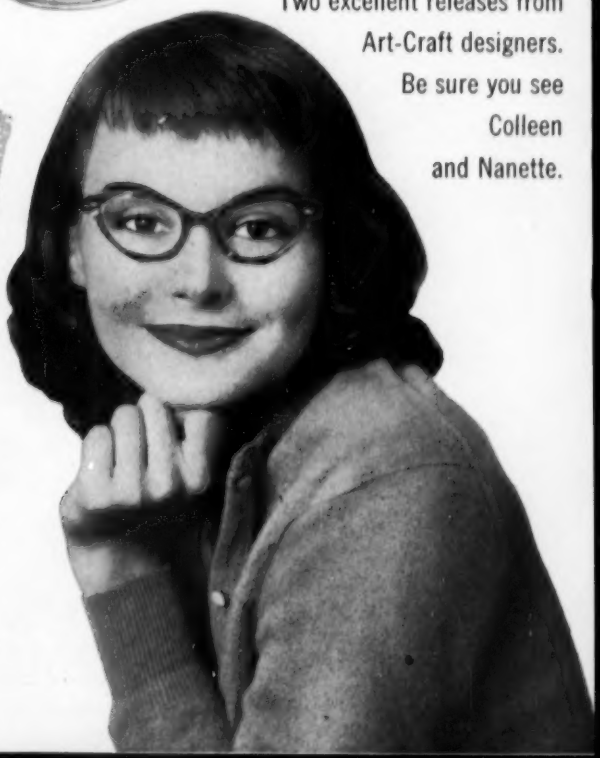
☆ The Nanette

Colors: *Mocha on Crystal, Cadet Blue on Crystal, Wine on Crystal, Blue Pearl on Crystal, Cherry Pearl on Crystal, Rose Pearl on Crystal, Mink Pearl on Crystal*

Available in both Clarbridge and Magicolor.

Two excellent releases from Art-Craft designers. Be sure you see Colleen and Nanette.

For Youth



☆ The Colleen

Colors: *Mocha on Crystal, Black on Crystal, Cadet Blue on Crystal, Mink Pearl on Crystal, Blue Pearl on Crystal, Cherry Pearl on Crystal, Rose Pearl on Crystal*

Available in both Clarbridge and Magicolor.

Art-Craft
OPTICAL COMPANY, INC.
• MANUFACTURERS •
89 Allen Street • Rochester 6, N. Y.

• DISTRIBUTED BY •

ART CRAFT OPTICAL OF NEW YORK CITY, INC. — ART CRAFT OPTICAL SOUTHEAST, INC.
ART CRAFT OPTICAL OF PHILADELPHIA, INC. — ART CRAFT OPTICAL OF ROCHESTER, INC.
ART CRAFT OPTICAL—MIDDLE ATLANTIC, INC. — ART CRAFT OPTICAL OF THE SOUTH, INC.
ART CRAFT OPTICAL OF NEW ENGLAND, INC. — ART CRAFT OPTICAL NORTH CENTRAL, INC.
ART CRAFT OPTICAL—MIDWEST, INC. — ART CRAFT OPTICAL OF CHICAGO, INC. — ART CRAFT OPTICAL—WEST COAST, INC.
ART CRAFT OPTICAL—SOUTHWEST, INC. — ART CRAFT OPTICAL EXPORT CORP. — ART CRAFT OPTICAL OF CANADA, LTD. — ART CRAFT OPTICAL—INTERAMERICANA, INC.

A Complete

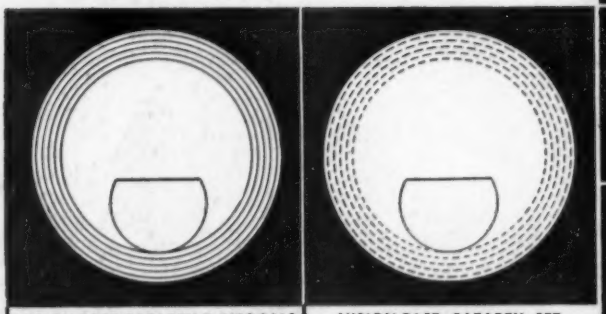
MULTIFOCAL SERVICE

for the

EXPANDING NEEDS

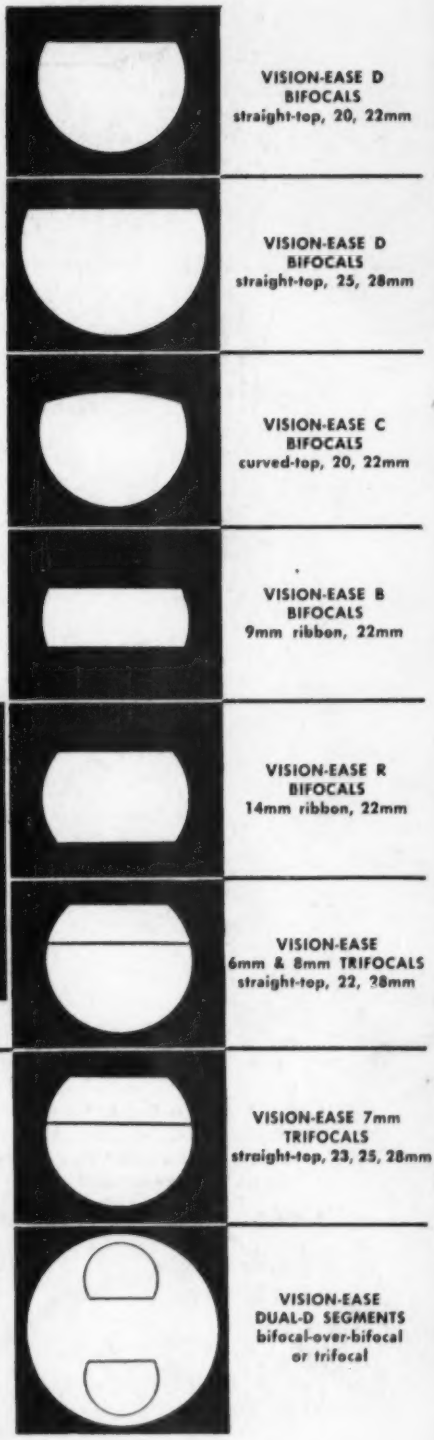
of the

PROFESSIONAL MAN!



VISION-EASE CATAREX D BIFOCALS
lenticular straight-top, 18mm

VISION-EASE CATAREX SET
temporary cataract bifocals



VISION-EASE D BIFOCALS
straight-top, 20, 22mm

VISION-EASE D BIFOCALS
straight-top, 25, 28mm

VISION-EASE C BIFOCALS
curved-top, 20, 22mm

VISION-EASE B BIFOCALS
9mm ribbon, 22mm

VISION-EASE R BIFOCALS
14mm ribbon, 22mm

VISION-EASE 6mm & 8mm TRIFOCALS
straight-top, 22, 28mm

VISION-EASE 7mm TRIFOCALS
straight-top, 23, 25, 28mm

VISION-EASE DUAL-D SEGMENTS
bifocal-over-bifocal or trifocal

THE

VISION-EASE

CORPORATION

Saint Cloud, Minnesota